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THE AGE-ORDER OF EPIPHYSIAL UNION IN BENGALEE GIRLS
(A Preliminary Study)

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The time of appearance and union of epiphysial centres of bones had, before the advent and perfection of clinical radiography, to be carried on in the post-mortem and dissection rooms and occasionally on the operation table. An analysis of the date on this subject as presented in the various text-books of anatomy, lately current, revealed a most striking divergency of opinion as to the actual time of union of the various epiphyses, the difference between the earliest and latest dates of such union, as given by different authors, being often as much as 11 years in particular cases. Even an anatomist like Elliot Smith had to admit that "in the present state of our knowledge, it would be rash and altogether unjustifiable to give in figures the precise age of a skeleton without making the reservation that it might be several years older or younger than the estimate."

While maceration of skeleton from individuals of precisely known age always remains the desideratum by which standards should be arrived at, it often becomes necessary for various purposes of medico-legal and scientific investigations to be sure of the presence of, or of the condition of union of, an epiphysial centre. With Röntgen's discovery of the x-rays the importance of such an enquiry struck Pryor in 1895 and with the help of x-rays he thought of corroborating or correcting the teaching of the time element in commencing ossification as given in text-books of anatomy. Pryor has, since then, been toiling on the subject. His lead has been taken up during the last ten years by investigators in America, (Wingate Todd, being pre-eminent in the field), England (Paterson and others), Prague (Borovansky and Hnevkovsky), Egypt (Sidhom and Derry), Australia (Flecker) and India (Hepworth, Galstaun, Pillai, Lall and Nat, and Barrett).

The radiological method presents certain advantages over the orthodox method of investigation by maceration. Stevenson has, of course, deprecated it by describing the skiagrams as 'merely a confusing medley of shadows.' But with care, chances of such confusion can certainly be reduced to a minimum. The chief advantage of the radiological method is that it can be used on the living person at any time, the behaviour of a particular epiphysis can be regularly followed in any particular subject and the average date of commencement or completion of union can be ascertained and compared with any

other similar case. The epiphysial centre can indeed be traced when it is no bigger than a pin's head and as such is likely to be lost in maceration. The fact can also be established beyond doubt that the subject for examination is normal and is not suffering from any pathological or endocrine disturbance. Besides, radiological methods when properly applied can be used as a delicate indicator in all conditions of defective calcium metabolism as reflected in the texture of bones, where other methods would scarcely be of much avail. Prof. Wingate Todd has in fact brought his method of "röntgenographic appraisement of human skeleton" to such a state of perfection that it has been accepted as a standard of health measurements by the White House Conference on Child Health and Protection called by President Hoover of U. S. A.

Though commendable work on the radiographic estimation of epiphysial union has been done by workers in Europe, America and elsewhere, in India, except for a recent paper of Galstaun which came out at the same time as the present paper was being written, very meagre attention has been paid to it so far. Hepworth (1929) was the first to bring out a paper here followed a year later by another by Galstaun. Both admitted that much more remained to be done. The works of Lall and Nat (1934), Barrett (1936) and Pillai (1936) are useful additional observations. Galstaun's recent work (1937) though presenting a large volume of creditable information does not take much notice of the fact that India is composed of different provinces each of which has its own climatic, dietetic and disease factors which leave on the skeletons of its people indelible marks that are widely different from the same from other provinces. Besides, the waves of migration of people and their scattering and intermingling that India had to witness since the early days of history, have made the basic racial stock in the provinces so divergent that wide generalisation of figures obtained indiscriminately should not only be unacceptable but positively dangerous to future workers.

Even in the same province a casual observer is struck by the difference in body nourishment in the several classes of its people. Taking Bengal, for example, it is found that the unbalanced nature of diet is the most remarkable fact not only amongst the poorest but also among the richest of her children. This has been amply illustrated in Dr. A. N. Chatterjee's "First Studies on Health and Growth of Bengalee Students". McCarrison and Akroyd's findings point to the deficiency of calcium, phosphorus and vitamins in the diet of Bengalees as being the chief factor responsible for their short size in comparison to the people of the Punjab, U. P. and Behar. Further, even amongst the people of Bengal the proximate principles of food differ so widely in the diet of the poor, middle and rich classes that it seems doubtful whether the same standard of epiphysial union should be retained as an universal measure for this province. The communal factor again, brings one more point for serious consideration. It requires to be solved whether the Christians and Mahomedans of Bengal with their more liberal diet unrestricted by religious considerations are placed in a more favourable position in this matter. Besides, one should not lose sight of the factor of 'heredity' as well as that of the endocrine preponderance in individual cases.

Scientists, however, should come to an agreed standard for the country or to such formulæ as can be utilised within limits for the determination of age of epiphysial union in the different provinces of India. The work of Hepworth, Galstaun and others in India is significant enough to warn us that we should not swear by European and American standards. The extensive observations of Prof. Wingate Todd teach us that dietetic differences, unless extreme, have not got much effect on the time of epiphysial union. This has to be verified on the different classes of people in this province. And, if scientists are able to set a standard for one province, say Bengal, and then carry on comparative work in other provinces of India, they will have made a comprehensive scientific basis with which they can start appraising any problem in this line of work.

One fact in epiphysial union, however, is certain and is admitted by all authorities the world over. It is that the female matures earlier than the males and consequently their epiphyses unite earlier. Since in this country the determination of age in females is often required to be done for medico-legal purposes, the authors of this paper in April, 1935, undertook as a preliminary measure an investigation of the condition in Bengalee girls.

The present work was started with the help of a small grant from the Department of Anatomy of the Carmichael Medical College. The

proprietors of Messrs. Basu Polyclinic, Calcutta, were kind enough to lend their x-ray apparatus and other appliances all through the work and in addition, bore a portion of the cost of materials and all other incidental expenses. The works could not have been possible without the encouragement and kind patronage of Dr. M. N. Bose, M.B., C.M. (Edin.), Principal and Professor of Anatomy of the Carmichael Medical College, Calcutta, who not only met a portion of the expenses from his own pocket, but was also instrumental in securing subsequent financial help from the Research Fund of the Carmichael Medical College.

130 subjects ranging from 3 to 19 years of age, have been examined for the present series and about 1300 skiagrams taken. The cases have been drawn chiefly from the middle class Bengalee families, only a very small percentage being from poor or rich families. Excepting one, who is a Bengalee Christian, all the others of the subjects are Bengalee Hindus living on a mixed diet.

To get at the correct age of the girls was the most difficult part of the task of the authors who had consequently to exclude all cases where any shadow of doubt existed as to the correct recording of the ages of the subjects. Almost invariably either of the authors would see with his own eyes the date of birth of the subjects as noted in their family records or in horoscopes. Simple oral statement was never relied upon. All attempts have been done to eliminate those cases who passed through long continued illness in their early life or who were very much under weight and under-sized or evinced definite pathological conditions.

In this paper the degree of union of the epiphysial centre with the diaphysis has been divided into three stages:

(1) Non-union—when there is a clear space between the epiphysis and diaphysis.

(2) Intermediate union—when the epiphysial space is partly filled by bone.

(3) Complete union—when no space is seen between the epiphysis and diaphysis and continuous bony strands are seen to pass from the one to the other. An epiphysial scar may remain for a long time after completion of fusion but this must not be confused with earlier stages of fusion.

As a matter of fact, it is generally agreed that when once the union of diaphysis and epiphysis starts at one point the whole process of fusion is completed in about six months. Hence all cases of 'intermediate union' may be taken as 'complete union' less six months, *i.e.* an addition of six months to the age of 'intermediate union' would bring it to the degree of 'complete union'.

The authors have, however, in the following tables taken regard of cases of 'complete union' only, both the remaining degrees being taken as 'non-union'.

TABLE 1

Fusion of Proximal Epiphysis of Humerus with the Shaft

Age.	No. of cases	No. of fusion	%age of fusion
7	... 1	nil	0
9	... 1	nil	0
10	... 1	nil	0
11	... 5	nil	0
12	... 13	nil	0
13	... 22	2	9·1
14	... 24	7	29·2
15	... 14	6	42·9
16	... 19	14	73·7
17	... 12	10	83·3
18	... 2	2	100
19	... 2	2	100

Hence, fusion is seen in the majority of cases between 16 and 17. Earliest fusion is seen in a case at 13 years and 9½ months. Latest non-fusion is seen in a case of 17 years and 7½ months. Text-books of anatomy give the time of fusion as 20-25. Flecker gives the time of fusion as 16-20. Galstaun gives the time of fusion as 14-16 years.

TABLE 2

Fusion of Lateral Epicondyle with the Shaft of Humerus

Age.	No. of cases	No. of fusion	%age of fusion
10	... 1	1	100
11	... 6	4	66·7
12	... 22	10	83·3
13	... 23	23	100
14 to 19	... 78	78	100

Hence, the age of fusion in the majority of cases is 12 to 13 years. According to Galstaun also it is 12 to 13 years.

TABLE 3

Fusion of Trochlea with Shaft of Humerus

Age.	No. of cases	No. of fusion	%age of fusion
10	... 1	nil	0
11	... 6	4	66·7
12	... 13	11	84·6
13	... 24	22	92·5
14	... 26	26	100
15 to 19	... 52	52	100

Hence, the majority of cases fuse between 12 and 13 years. Galstaun's figure also is 12 to 13 years.

TABLE 4

Fusion of the compound centre for Capitellum, Trochlea and Lateral Epicondyle with the Shaft of Humerus

Age.	No. of cases	No. of fusion	%age of fusion
3	... 1	nil	0
5	... 1	nil	0
9	... 2	nil	0
10	... 2	nil	0
11	... 6	2	33·3
12	... 14	10	71·4
13	... 23	23	100
14	... 26	26	100
15	... 14	14	100
16	... 20	20	100
17	... 12	12	100
18	... 3	3	100
19	... 3	3	100

Hence, the majority of cases fuse between 12 and 13 years. Earliest fusion has been seen at 11 years five months. Latest non-fusion has been seen at 12 years 7 months.

TABLE 5

Epiphysis for Medial Epicondyle of Humerus

Age.	No. of cases	No. of fusion	%age of fusion
5	... 1	nil	0
9	... 2	nil	0
10	... 1	nil	0
11	... 6	1	16·7
12	... 12	1	8·3
13	... 23	12	52·2
14	... 26	24	92·3
15	... 14	13	92·8
16	... 20	20	100
17	... 12	11	91·7
18	... 3	3	100
19	... 3	3	100

Hence, the majority of cases fuse between 13 and 14 years. Galstaun puts it at 14 to 15 years.

Earliest fusion noticed at 11 years 11 months and latest non-fusion noticed at 17 years 4½ months.

TABLE 6

Proximal Epiphysis of Radius

Age.	No. of cases	No. of fusion	%age of fusion
3	... 1	nil	0
9	... 4	nil	0
11	... 6	1	16·7
12	... 14	4	28·6
13	... 23	17	74
14	... 26	24	92·3
15	... 14	13	93
16	... 20	20	100
17 to 20	... 18	18	100

Hence, the majority of cases fuse at 13 to 14 years, Galstaun puts it at 14. Earliest fusion is seen at 11 years 11 months and latest non-fusion seen at 15 years 8½ months.

TABLE 7

Proximal Epiphysis of Ulna

Age.	No. of cases	No. of fusion	%age of fusion
9	... 2	nil	0
10	... 1	nil	0
11	... 6	1	16·7
12	... 14	5	35·7
13	... 23	19	82·2
14	... 26	25	96·2
15	... 14	14	100
16	... 20	20	100
17	... 12	12	100
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is seen at 13 to 14 years. Galstaun places it at 15 years. Earliest fusion is seen at 11 years 11 months, latest non-fusion at 13 years 5 months.

TABLE 8

Distal Epiphysis of Radius

Age.	No. of cases	No. of fusion	%age of fusion
3	... 1	nil	0
5	... 1	nil	0
9	... 2	nil	0
10	... 2	nil	0
11	... 21	nil	0
13	... 22	1	4·5
14	... 26	4	15·4
15	... 14	4	28·6
16	... 20	16	80
17	... 12	9	75
18	... 3	3	100
19	... 3	3	100

Hence, the majority of cases are seen to fuse between the 16th and 17th year. Paterson places it at 20, Flecker at 18 and Galstaun at 16½ years. Earliest fusion is seen at 13 years 7 months latest non-fusion seen at 17 years 7½ months.

TABLE 9

Distal Epiphysis of Ulna

Age.	No. of cases	No. of fusion	%age of fusion
9	... 2	nil	0
10	... 2	nil	0
11	... 6	nil	0
12	... 15	nil	0
13	... 22	2	9·1
14	... 26	10	38·5
15	... 14	6	42·9
16	... 20	16	80
17	... 12	10	83·3
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is between 16 and 17 years. Galstaun puts it at 17 years. Earliest fusion is seen at 13 years 7 months, latest non-fusion at 17 years 7½ months.

TABLE 10

The Pisiform Bone

Age.	No. of cases	Appearance of centre in	%age of appearance.
3	... 1	nil	0
5	... 1	nil	0
9	... 2	1	50
10	... 2	1	50
11	... 6	6	100
12	... 12	12	100
13 to 19	... 69	69	100

Hence, the centre is present in the majority of cases after the 10th year and is always present after the 11th year. Galstaun ascribes universal presence of this bone at the 12th year.

TABLE 11

Epiphysis for base of First Metacarpal

Age.	No. of cases	No. of fusion	%age of fusion
3 to 10	... 5	nil	0
11	... 6	1	16·7
12	... 15	3	20
13	... 22	9	40·9
14	... 26	24	92·3
15	... 14	11	78·6
16	... 20	20	100
17	... 12	11	91·7
18	... 3	3	100
19	... 3	3	100

Hence, the majority of cases are seen to fuse at the age of 14., Galstaun's figures agree with this finding. Earliest fusion seen at 11 years, 11 months, latest non-fusion at 17 years 4½ months. In none of these cases the authors could find an epiphysial centre for the head of the first metacarpal.

TABLE 12

Distal Phalanx of thumb

Age.	No. of cases	No. of fusion	%age of fusion
5	... 1	nil	0
9	... 2	nil	0
10	... 2	nil	0
11	... 6	1	16·7
12	... 12	4	33·3
13	... 15	11	73·3
14	... 15	14	93·3
15	... 7	7	100
16	... 18	18	100
17	... 10	10	100
18	... 2	2	100
19	... 2	2	100

Hence, the age of fusion in the majority of cases is between 13 to 14 years. Galstaun puts it at 14 and 16, Flecker 15-16, Paterson at 17. Earliest fusion is seen at 11 years 11 months, latest non-fusion at 14 years 3 months.

TABLE 13

Epiphysis for Head of Femur

Age.	No. of cases	No. of fusion	%age of fusion
7	... 1	nil	0
10	... 2	nil	0
11	... 3	2	66·7
12	... 10	3	30
13	... 22	15	68·1
14	... 25	24	96
15	... 13	12	92·3
16	... 19	19	100
17	... 12	12	100
18	... 3	3	100
19	... 3	3	100

Hence, union occurs in the majority of cases at 13 to 14 years. Galstaun gives it at 14 to 15 years, Paterson at 17 and Flecker at 14. Text-books on anatomy place it between 18 and 20. Earliest fusion is noticed in a case at 11 years 5 months, latest non-fusion is noticed in a case at 15 years 8½ months.

TABLE 14

Epiphysis for Lesser Trochanter of Femur

Age.	No. of cases	No. of fusion	%age of fusion
11	... 2	1	50
12	... 5	2	40
13	... 9	8	88·9
14	... 12	12	100
15	... 5	5	100
16	... 8	8	100
17	... 7	6	85
18	... 1	1	100
19	... 2	2	100

Therefore, age of fusion in the majority of cases is 13. Galstaun and other authorities put it at 15 to 17 years. Earliest fusion is seen at 11 years 11 months and latest non-fusion seen at 17 years 4½ months.

TABLE 15

Epiphysis for Greater Trochanter of Femur

Age.	No. of cases	No. of fusion	%age of fusion
7	... 1	nil	0
10	... 2	nil	0
11	... 3	nil	0
12	... 9	2	22·2
13	... 20	8	40
14	... 25	22	88
15	... 13	10	76·9
16	... 20	20	100
17	... 12	11	91·7
18	... 3	3	100
19	... 3	3	100

Fusion occurs in the majority of cases at 14 years. Galstaun gives the figure at 14, Paterson at 16-17 and Flecker at 14-15 years. Earliest fusion is noticed in a case at 12 years 7½ months, latest non-fusion noticed in a case at 17 years 4½ months.

TABLE 16

Distal Epiphysis of Femur

Age.	No. of cases	No. of fusion	%age of fusion
9	... 1	nil	0
10	... 1	nil	0
11	... 4	nil	0
12	... 10	nil	0
13	... 21	3	14·3
14	... 24	8	33·3
15	... 13	4	30·8
16	... 19	17	84·5
17	... 12	10	83·3
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is 16 years. Galstaun gives the figures at 14, Paterson at 16 and Flecker at 17 years. Earliest fusion is seen in a case at 13 years 7 months; latest non-fusion is seen in a case at 17 years 7½ months.

TABLE 17

Proximal Epiphysis of Tibia

Age.	No. of cases	No. of fusion	%age of fusion
9	... 1	nil	0
10	... 2	nil	0
11	... 4	nil	0
12	... 10	nil	0
13	... 21	4	19·5
14	... 24	12	50
15	... 13	9	69·2
16	... 18	17	94·4
17	... 12	10	83·3
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is at 15 to 16 years. Galstaun's figures place the age at 14-15, Flecker at 15, Paterson at 16-17. Earliest fusion is seen at 13 years 7 months, latest non-fusion at 17 years 7½ months.

TABLE 18

Proximal Epiphysis of Fibula

Age.	No. of cases	No. of fusion	%age of fusion
9	... 1	nil	0
10	... 1	nil	0
11	... 4	nil	0
12	... 10	nil	0
13	... 20	2	10
14	... 24	6	25
15	... 13	5	38·5
16	... 17	13	76·5
17	... 12	10	83·3
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is 16 to 17 years. Flecker puts the age at 15 and Galstaun and Paterson at 16. Earliest fusion is seen at 13 years 7 months and latest non-fusion seen up to 17 years 7½ months.

TABLE 19

Distal Epiphysis of Fibula

Age.	No. of cases	No. of fusion	%age of fusion
9	... 1	nil	0
10	... 2	nil	0
11	... 5	nil	0
12	... 11	1	9·1
13	... 22	5	22·7
14	... 25	14	56
15	... 13	11	84·6
16	... 20	18	90
17	... 12	11	91·7
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is at 15 years. Flecker puts it at 14·1, Galstaun at 14·3 and Paterson at 16 years. Earliest fusion is seen at 12 years 9½ months, latest non-fusion at 15 years 8½ months.

TABLE 20

Distal Epiphysis of Tibia

Age.	No. of cases	No. of fusion	%age of fusion
9	... 1	nil	0
10	... 2	nil	0
11	... 5	nil	0
12	... 11	1	9·1
13	... 22	7	31·8
14	... 24	18	75
15	... 13	11	84·6
16	... 19	19	100
17	... 12	11	91·7
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is 14 to 15 years. Flecker puts the age at 14, Galstaun at 15 and Paterson at 16 years. Earliest fusion is seen at 12 years 9½ months and latest non-fusion at 17 years 4½ months.

TABLE 21

Calcaneal Epiphysis

Age.	No. of cases	No. of fusion	%age of fusion
9	... 1	nil	0
10	... 2	nil	0
11	... 5	2	40
12	... 11	1	9·1
13	... 21	11	52·4
14	... 24	22	91·7
15	... 14	14	100
16	... 18	18	100
17	... 12	12	100
18	... 3	3	100
19	... 3	3	100

Hence, the age of fusion in the majority of cases is between 13 and 14 years. Galstaun puts it at 14. Earliest fusion is seen at 11 years 5 months and latest non-fusion at 14 years 3 months.

CONCLUSION

From a study of the foregoing tables it will be found that considerable discrepancy exists between results arrived at independently by the present authors and those in Galstaun's work just published. Paterson's figures, however, are usually higher by a couple of years. Flecker's figures for Australian girls, curiously, very often agree with the results of the present series. All the authors, however, are unanimously of opinion that the figures given in textbooks are very high and must be readjusted in the light of modern investigations. A concluding table (Table 22) is given where the authors present at one place the ages at which the epiphyses unite with the diaphyses in the case of the majority of Bengalee girls.

TABLE 22

Epiphyses	Age (in years) of union in majority of Bengalee girls.
Proximal, humerus	16 to 17
Lateral epicondyle with shaft of humerus	12 to 13
Trochlea with shaft of humerus	12 to 13
Compound centre for lower epiphysis with shaft of humerus	12 to 13
Medial epicondyle of humerus	13 to 14
Proximal, radius	13 to 14
Proximal, ulna	13 to 14
Distal, radius	16 to 17
Distal, ulna	16 to 17
Pisiform, centre present at	11 & upwards
Base, first metacarpal	14
Distal phalanx, thumb	13 to 14
Head, femur	13 to 14
Lesser trochanter, femur	13
Greater trochanter, femur	14
Distal, femur	16
Proximal, tibia	15 to 16
Proximal, fibula	16 to 17
Distal, tibia	14 to 15
Distal, fibula	15
Apophysis, calcaneus	14 to 15

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OBSERVATIONS ON DETERIORATION OF PHYSIOLOGICAL ACTIVITY OF TINCTURE DIGITALIS

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Although several papers have been published in the medical journals from time to time on the effect of aging of digitalis preparations, the subject of deterioration of their physiologically active principles is still far from being completely settled. For on one side we have the evidence of pioneer bio-assayists like Hatcher and Eggleston (1913), who concluded that, as measured by the cat method, good quality digitalis leaves did not deteriorate more rapidly than 1·5 to 2 per cent. a year and galenical preparations containing at least 50 per cent. of alcohol were also stable. On the other side we get the opposite view of Tate (1921), Chopra, Bose and Dey (1925) and Bhatia (1933) that tincture of digitalis deteriorates very rapidly, specially in the warm climate of India. Wokes (1930), again, has an interesting finding that tincture of digitalis deteriorates at the rate of 3 per cent. per month when examined by the frog method, but no deterioration is detected at all by the cat method. Foster (1937) in a second paper on the subject declared before the American Society of Pharmacology and Experimental Therapeutics that while six-years old samples of absolute alcohol tincture digitalis indicate no change in potency, assays on tinctures prepared by cold percolation show increased activity after six years' standing. The position, it seems, has been rightly summed up in the Quarterly Bulletin of the Health Organisation of the League of Nations (Volume IV, No. 3, September, 1935, page 522):—

> "Some uncertainty still prevailed in regard to the assay of digitalis. In the first place, it had not been demonstrated that the active principles measured by the different methods were the same. Secondly, it remained to be determined which method would yield the most accurate titration of the active principle responsible for the therapeutic effect of digitalis. The therapeutic tests performed with three samples of digitalis on patients suffering from heart disease in the hospitals at Edinburgh and Baltimore, showed that it was not possible to arrive at any quantitative appraisal of the action of digitalis preparation through tests on human beings by present-day clinical methods. The only inference that could be drawn from these experiments was that the sample which was least active on animals also produced the least effect on man. It would seem, therefore, from a clinician's standpoint, that there is no need to assay digitalis preparations with strict accuracy; and that digitalis leaves whose activity is within ±25 per cent. of that of the standard preparation would satisfy therapeutic requirements".

With a view to see if any further light can be thrown on this very interesting problem, the present writer, who has ample opportunities and has to standarise on an average about 70 to 80 samples of tincture digitalis every year, undertook to investigate the question once again. His three years' careful observations on 112 samples in one series and 13 in another are now faithfully recorded.

Method of Assay

Samples of B. P. Tincture, obtained from the manufacturers (B. C. P. W.) in ordinary 2 oz. phials, were kept separate in an open shelf of the laboratory, well-corked and paraffined. No other precaution was taken. They were assayed against a standard tincture prepared from 'Standard Digitalis Powder' (1928) of the National Institute for Medical Research, London. In the actual assay, Dr. Burn's cat method was followed with slight modification. The tinctures, both the Standard and the Unknown, were diluted 20

times with 0·9 per cent. saline and injected at a constant rate, approximately 1 c.c. in 2 minutes, into a series of three cats (non-pregnant and non-lactating), anæsthetised three hours previously with intramuscular injection of urethane in a dose of 1·8 gm. per Kg. dissolved in warm water. The injection was made into the femoral vein of one side and the blood pressure was recorded from the carotid artery. The endpoint was determined when the sharp drop in the blood pressure indicated that the digitalis had reached such a concentration in the heart muscle, that the heart had stopped in systolic contraction. The potency of the sample was determined in comparison with that of the standard tincture, which, however, was assayed once in a month.

TABLE 1 : records assay results of 112 samples: of these 50 samples have been re-assayed three times (at the end of 1st, 2nd and 3rd year), 83 twice (1st and 2nd year) and 29 only once (1st year).

TABLE 2: assay results of 13 samples, obtained from local chemists. Their approximate age was roughly determined from the indent books of the firms concerned.

The experiments and their results speak for themselves and there is very little to discuss. The cat method of assay is simple, speedy and still believed by the majority of workers to be the best. For, cats, unlike frogs and pigeons, do not vary markedly in sensitiveness to digitalis at different times of the year and there is no need to make simultaneous tests of the Standard and the Unknown. Once the average lethal dose of the Standard tincture per Kg. cat is determined, it can be safely compared with that obtained in a large number of subsequent experiments with the Unknown (Burn). The "Standard Digitalis Powder (1928)" was used throughout, even after the "1936 Powder" was issued, first, because the latter was not available from the beginning of these experiments and secondly, because what was primarily aimed at was comparative results and not accurate potency figures. It should also be pointed out that neither Trevan's original suggestion of using 20 cats (14 for Standard and 6 for Unknown), nor that of Burn's 10 cats (5 and 5) could be carried out. Cats have become rather scarce in these parts.

DIFFICULTY OF BIO-ASSAY

A few words regarding variability of bio-assay results may not be out of place here. Results vary not only with different species of animals, such as dogs, cats, pigeons and frogs, but even in a particular method, with such factors as (a) nature of anæsthetics used (E-C mixture, chloretone, urethane, etc.), (b) time spent on experiments, (c) number and sensitiveness of animals, and (d) the potency of the Standard selected. Indeed the last factor very often proves a difficult one. The British Council of Medical Research distributes the "Standard Digitalis Powder", but the actual tincture has got to be locally perpared for comparison with the Unknown and herein lies a potent source of error. For unlike a soluble salt, a given quantity of digitalis powder may not always yield identical quantities of active principle. Much will depend on the quality of the solvent used, time given for solution and other technical details. It is quite plain, therefore, that if the Standard is not properly prepared and matured, the comparison is bound to be fallacious. Dr. Burn concludes—"It is evident that the relative sensitiveness to different digitalis glucosides differs in different species, and we are faced with the problem of discovering which method gives the right answer. There is no way of doing this save to make a careful comparison of different tinctures on a large number of patients. Some attempts of this kind have been made, but the results are inconclusive. Notwithstanding this difficulty, the biological standardisation is valuable in preventing the use of adulterated leaf or leaf of very low activity for the treatment of heart disease".

SUMMARY

1. One hundred and twelve samples of Tincture Digitalis P. B. were biologically assayed and re-assayed against the Standard Tincture by a slightly modified method of Dr. Burn (Cat Method).

2. Of these:—

(a) 8 per cent. samples show deterioration 10-15 per cent. at the end of the first year.

(b) 21 per cent. samples show deterioration 15-20 per cent. at the end of the second year.

(c) 56 per cent. samples show deterioration 20-40 per cent. at the end of the third year.

TABLE 1

DETERIORATION OF TINCTURE DIGITALIS P. B. (B. C. P. W.)

By Cat Method—Burn.

When first assayed				Assayed after 12 months			Assayed after 24 months.			Assayed after 36 months		
No.	Sample	Date	Potency*	Date	Potency*	Change, if any	Date	Potency*	Deterioration	Date	Potency*	Deterioration
1	618	9-1-34	85·7	11-1-35	80	− 5·9	9-1-36	72	−13·7	11-1-37	55	−30·7
2	621	11-1-34	100	12-1-35	95	− 5	13-1-36	84	−16	16-1-37	82	−18
3	631	10-2-34	91·6	12-2-35	80	−11·6	10-2-36	80	−11·6	8-2-37	57	−34·6
4	633	12-2-34	85·1	13-2-35	82	− 3·1	13-2-36	80	− 5·1	12-2-37	75	−10·1
5	644	9-3-34	118·1	9-3-35	120	+ 1·9	12-2-36	110	− 8·1	12-3-37	80	−38·1
6	645	10-3-34	91·6	18-3-35	95	+ 3·4	16-3-36	78	−13·6	17-3-37	52	−39·6
7	649	16-3-34	114·1	18-3-35	110	− 4·1	16-3-36	95	−19·1	17-3-37	95	−19·1
8	652	19-3-34	84	21-3-35	80	− 4	20-3-36	76	− 8	22-3-37	66	−18
9	661	4-4-34	108·6	5-4-35	110	+ 1·4	4-4-36	90	−18·6	5-4-37	68	−40·6
10	664	6-4-34	85	9-4-35	83	− 2	7-4-36	75	−10	6-4-37	50	−35
11	673	23-4-34	137·7	24-4-35	130	− 7·7	27-4-36	120	−17·7	22-4-37	118	−19·7
12	684	3-5-34	89·6	7-5-35	80	− 9·6	8-5-36	80	− 9·6	5-5-37	72	−17·6
13	687	9-5-34	140	10-5-35	135	− 5	12-5-36	135	− 5	10-5-37	100	−40
14	691	12-5-34	92·8	13-5-35	95	+ 2·2	14-5 36	90	− 2·8	14-5-37	60	−32·8
15	696	21-5-34	94·4	22-5-35	95	+ 0·6	20-5-36	84	−10·4	24-5-37	60	−34·4
16	697	22-5-34	113·3	24-5-35	110	− 3·3	25-5-36	100	−13·3	27-5-37	95	−18·3
17	700	26-5-34	122·2	27-5-35	115	− 7·2	25-5-36	120	− 2·2	28-5-37	84	−38·2
18	709	11-6-34	125	12-6-35	120	− 5	10-6-36	105	−20	14-6-37	85	−40
19	731	6-7-34	87·1	6-7-35	90	+ 2·9	8-7-36	80	− 7·1	10-7-37	75	−12·1
20	733	7-7-34	100	9-7-35	98	− 2	10-7-36	95	− 5	13-7-37	82	−18
21	742	17-7-34	125	19-7-35	128	+ 3	17-7-36	116	− 9	14-7-37	87	−38
22	749	23-7-34	111	24-7-35	110	− 1	25-7-36	100	−11	24-7-37	95	−16
23	759	8-8-34	87·5	10-8-35	85	− 2·5	8-8-36	80	− 7·5	9-8-37	50	−37·5
24	762	21-8-34	100	22-8-35	87	−13	27-8-36	80	−20	23-8-37	83	−17
25	764	24-8-34	90	28-8-35	87	− 3	31-8-36	78	−12	25-8-37	50	−40
26	783	15-9-34	80	14-9-35	82	+ 2	18-9-36	68	−12	17-9-37	50	−30
27	793	29-9-34	80	30-9-35	85	+ 5	28-9-36	75	− 5	1-10-37	45	−35
28	798	10-10-34	125	18-10-35	120	− 5	14-10-36	106	−19	26-10-37	85	−40
29	804	30-10-34	116·6	30-10-35	110	− 6·6	11-11-36	100	−16·6	30-10-37	76·6	−40
30	808	3-11-34	113·3	4-11-35	110	− 3·3	12-11-36	100	−13·3	6-11-37	95	−18·3
31	819	13-11-34	95	13-11-35	90	− 5	16-11-36	83	−12	16-11-37	58	−37
32	821	17-11-34	93·7	19-11-35	90	− 3·7	20-11-36	85	− 8·7	19-11-37	80	−13·7
33	849	17-12-34	88·8	18-11-35	82	− 6·8	17-12-36	80	− 8·9	18-12-37	72	−16·8
34	853	20-12-34	87·5	20-12-35	85	− 2·5	18-12-36	80	− 7·5	21-12-37	70	−17·5

* Potency compared with that of Standard Tincture, 100.

TABLE 1—(*Contd.*)

When first assayed				Assayed after 12 months			Assayed after 24 months.			Assayed after 36 months		
No.	Sample	Date	Potency*	Date	Potency*	Change, if any	Date	Potency*	Deterioration	Date	Potency*	Deterioration
35	861	28-12-34	100	27-12-35	105	+ 5	29-12-36	98	− 2	29-12-37	61	−39
36	872	11-1-35	118·1	13-1-36	115	− 3·1	13-1-37	100	−18·1	10-1-38	99	−19·1
37	879	17-1-35	122	17-1-36	111	−11	16-1-37	115	− 7	17-1-38	110	−12
38	889	23-1-35	84·6	24-1-36	80	− 4·6	28-1-37	80	− 4·6	24-1-38	68	−16·6
39	908	4-2-35	122	5-2-36	120	− 2	5-2-37	104	−18	3-2-38	84	−38
40	915	15-2-35	120	18-2-36	122	+ 2	17-2-37	100	−20	16-2-38	80	−40
41	917	16-2-35	100	20-2-36	105	+ 5	18-2-37	100	Nil	17-2-38	64	−36
42	936	4-3-35	87·5	6-3-36	85	− 2·5	3-3-37	82	− 5·5	5-3-38	75	−12·5
43	942	6-3-35	82·7	12-3-36	80	− 2·7	13-3-37	76	− 6·7	7-3-38	50	−32·7
44	943	9-3-35	127·7	13-3-36	115	−12·7	15-3-37	115	−12·7	10-3-38	90	−37·7
45	956	27-3-35	100	26-3-36	95	− 5	31-3-37	83	−17	28-3-38	61	−39
46	974	15-4-35	81·4	17-4-36	80	− 1·4	16-4-37	68	−13·4	19-4-38	45	−36·4
47	1000	10-5-35	92·3	12-5-36	81	−11·3	14-5-37	80	−12·3	11-5-38	54	−38·3
48	1009	15-5-35	118·7	16-5-36	105	−13·7	17-5-37	102	−16·7	18-5-38	100	−18·7
49	1018	21-5-35	137·5	20-5-36	130	− 7·5	21-5-37	135	− 2·5	23-5-38	120	−17·5
50	1026	30-5-35	128	1-6-36	120	− 8	31-5-37	115	−13	27-5-38	110	−18
51	1054	26-6-35	100	26-6-36	102	+ 2	22-6-37	87	−13			
52	1057	28-6-36	100	2-7-36	96	− 4	25-6-37	83	−17			
53	1065	6-7-35	125	8-7-36	120	− 5	7-7-37	115	−10			
54	1075	16-7-35	81·8	17-7-36	83	+ 1·2	17-7-37	70	−11·8			
55	1096	9-8-35	90	10-8-36	95	+ 5	9-8-37	77	−13			
56	1100	12-8-35	90·6	13-8-36	95	+ 4·4	14-8-37	80	−10·6			
57	1107	19-8-35	113·3	21-8-36	110	− 3·3	19-8-37	98	−15·3			
58	1111	20-8-35	89·4	22-8-36	88	− 1·4	21-8-37	80	− 9·4			
59	1116	28-8-35	100	31-8-36	102	+ 2	28-8-37	86	−14			
60	1122	5-9-35	100	8-9-36	105	+ 5	10-9-37	86	−14			
61	1135	11-9-35	81·8	12-9-36	86	+ 5·8	11-9-37	70	−11·8			
62	1159	22-10-35	112·5	17-10-36	108	− 4·5	30-10-37	110	− 2·5			
63	1160	22-10-35	100	17-10-36	102	+ 2	4-11-37	95	− 5			
64	1166	30-10-35	112·5	9-11-36	115	+ 2·5	6-11-37	100	−12·5			
65	1169	4-11-35	107·1	11-11-36	115	+ 7·9	8-11-37	97	−10·1			
66	1182	16-11-35	131·2	16-11-36	125	− 6·2	17-11-37	118	−13·2			
67	1185	19-11-35	125	20-11-36	125	Nil	19-11-37	120	− 5			
68	1188	27-11-35	100	30-11-36	100	Nil	22-11-37	87	−13			
69	1203	12-12-35	134·7	14-12-36	122	−12·7	13-12-37	118	−16·7			
70	1213	20-12-35	100	21-12-36	95	− 5	20-12-37	88	−12			
71	1221	2-1-36	89·4	4-1-37	92	+ 2·6	3-1-38	80	− 9·4			
72	1222	4-1-36	128	5-1-37	125	− 3	4-1-38	108	−20			
73	1243	24-1-36	85·1	22-1-37	95	+ 9·9	24-1-38	80	− 5·1			

* Potency compared with that of Standard Tincture, 100.

TABLE 1—(*Contd.*)

TABLE 1—(*Contd.*)

When first assayed				Assayed after 12 months			Assayed after 24 months.		
No.	Sample	Date	Potency*	Date	Potency*	Change, if any	Date.	Potency*	Deterioration
74	1257	18-2-36	93·3	23-1-37	98	+ 4·7	25-1-38	80	−13·3
75	1263	24-2-36	96	23-2-37	90	− 6	18-2-38	85	−11
76	1273	18-3-36	95	17-3-37	90	− 5	18-3-38	92	− 3
77	1275	21-3-36	84·6	22-3-37	100	+15·4	22-3-38	75	− 9·6
78	1279	24-3-36	120	23-3-37	125	+ 5	25-3-38	111	− 9
79	1282	28-3-36	100	31-3-37	111	+11	26-3-38	86	−14
80	1284	31-3-36	88	2-4-37	92	+ 4	28-3-38	77	−11
81	1294	8-4-36	96·4	9-4-37	90	− 6·4	11-4-38	84	−12·4
82	1297	17-4-36	115	20-4-37	110	− 5	21-4-38	95	−20
83	1302	30-4-36	100	30-4-37	102	+ 2	29-4-38	87	−13
84	1315	12-5-36	111·1	14-5-37	105	− 6·2			
85	1324	22-5-36	90·9	21-5-37	85	− 5·9			
86	1337	9-6-36	85·7	10-6-37	85	− 0·7			
87	1341	24-6-36	122·2	23-6-37	115	− 7·2			
88	1355	10-7-36	88·8	10-7-37	82	− 6·8			
89	1358	20-7-36	94·1	19-7-37	95	+ 0·9			
90	1365	29-7-36	100	27-7-37	96	− 6			
91	1367	29-7-36	114·2	28-7-37	115	+ 0·8			
92	1369	31-7-36	116·6	31-7-37	115	− 1·6			
93	1374	8-8-36	122·2	9-8-37	118	− 4·2			
94	1380	14-8-36	84	17-8-37	90	+ 6			
95	1387	22-8-36	89·4	24-8-37	80	− 9·4			
96	1391	27-8-36	100	25-8-37	97	− 3			
97	1398	8-9-36	116·6	7-9-37	102	−14·6			
98	1405	14-9-36	107·1	17-9-37	100	− 7·1			
99	1414	23-9-36	100	25-9-37	100	Nil			
100	1421	1-10-36	133·3	2-10-37	140	+ 6·7			
101	1422	5-10-36	88·2	6-10-37	82	− 6·2			
102	1433	14-10-36	100	26-10-37	92	− 8			
103	1440	17-10-36	115	27-10-37	120	+ 5			
104	1443	9-11-36	91·6	8-11-37	80	−11·6			
105	1446	11-11-36	93·3	13-11-37	90	− 3·3			
106	1450	18-11-36	112·5	19-11-37	115	+ 2·5			
107	1459	5-12-36	95	4-12-37	90	− 5			
108	1464	9-12-36	86·2	11-12-37	80	− 6·2			
109	1476	11-12-36	93·3	14-12-37	90	− 3·3			
110	1478	21-12-36	125	20-12-37	112	−13			
111	1482	28-12-36	82	27-12-37	80	− 2			
112	1485	31-12-36	83·3	29-12-37	85	+ 1·7			

* Potency compared with that of Standard Tincture, 100.

TABLE 2

TINC. DIGITALIS P. B. (B. C. P. W.) FROM LOCAL CHEMISTS

Approximate date of indent by the Chemists concerned	Age of Tinc. not less than	As assayed	
		On	Potency*
August, 1934	... 3 yrs.	3-7-37	102·3
September, 1935	... 2 yrs.	7-7-37	88·8
February, 1932	... 6 yrs.	9-7-37	40·6
May, 1935	... 2 yrs.	10-7-37	·84·3
? 1934	... 3 yrs.	14-7-37	109·5
August, 1936	... 1 yr.	16-7-37	102·7
October, 1935	... 2 yrs.	4-10-37	93·7
January, 1936	... 2 yrs.	7-4-38	116
January, 1936	... 2 yrs.	15-4-38	111
April, 1935	... 3 yrs.	6-5-38	100
January, 1933	... 5 yrs.	9-5-38	65
February, 1937	... 1 yr.	11-5-38	95
August, 1935	... 3 yrs.	14-5-38	80

* Compared with that of the Standard Tincture, 100.

3. Of the thirteen samples from the local chemists at Calcutta, all, except two (more than 5 years old), were potent.

4. If the accepted principle of the Biological Standardisation Committee of the League of Nations is to pass as satisfactory tinctures that do not differ from the standard by more than ± 25 per cent. the results of these experiments would seem to indicate that tincture digitalis remains fairly potent at least for two years even in the warm climate of India.

5. Attention has been drawn to the difficulties of bio-assay of digitalis preparations and assessment of their therapeutic value.

In conclusion, the writer wishes to acknowledge his indebtedness to the authorities of the Bengal Chemical & Pharmaceutical Works, Ld., particularly to the Manager, Mr. J. N. Lahiri, for their liberal assistance rendered in connection with these experiments. He is also grateful to his technical assistant Mr. M. Roy.

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RECENT STUDIES ON STAPHYLOCOCCUS PYOGENES WITH PARTICULAR REFERENCE TO ITS EXOTOXIN, ANATOXIN AND ANTITOXIN

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It was near about 1880 that staphylococcus came into existence in the field of bacteriology. It was first observed by Koch in 1878 and was first cultivated in a fluid medium by Pasteur in 1880. Ogston (1882) and Rosenbach (1884) made a further study of this organism. Since then, it has become known to be a common pyogenic organism. Staphylococcus has been held to be the primary agent of causing many trifling and some severe diseases such as boils, furunculosis, whitlows, carbuncles, cellulitis, osteomyelitis etc., though in graver condition of some such diseases, the combined action of streptococcus pyogenes whether actually present or not, used to be always suspected on account of the prevalent idea of the less pathogenic and toxic nature of staphylococcus. It is also commonly found as a secondary infection in some skin lesions such as eczema, acne, etc., in nasal catarrh and in the genito-urinary tract but much importance has never been attached to these secondany invaders. The pathogenic power of staphylococcus pyogenes was believed to be solely due to their endotoxin alone and as a remedial measure, Wright and his school strongly advocated the vaccine therapy which has long been widely used with more or little success in cases of all sorts of staphylococcus infections.

Only on rare occasions, staphylococcus was considered to be a fatal agent. This micro-organism used to be so lightly treated in comparison with streptococcus pyogenes that even in actual septicæmia cases, staphylococcus found in blood culture was often taken to be a common contaminating organism and blood culture was, in many cases, repeated in search for streptococcus hæmolyticus. The laboratory findings of staphylococcus aureus alone in the cultural result of pus from severe cases of carbuncles, cellulitis etc., used to be accepted not seriously and in spite of the repeated reports of the absence of streptococcus in the cultural finding, massive doses of anti-streptococcal serum used to be administered with disappointing result. In this connection it may be mentioned that, while work with staphylococcal exotoxin considerably advanced elsewhere and the preparation of staphylococcal antitoxin was an established fact, here, in India, Chatterjee and De (1936) published a paper after an elaborate study on "Facial Cellulitis" in which the authors had, at last, boldly stated that "with the idea that all these cases, exhibiting severe toxæmia, are infections caused by streptococci, large quantities of polyvalent streptococcal serum are used. It is difficult to trace the reason for this belief. Probably the bacteriology of the disease is not accurately appreciated". Such was the state of our imperfect knowledge about the real pathogenic and virulent nature of staphylococcus pyogenes, up till very recently.

Towards the close of the last century, there was, of course, some incomplete study in the toxic nature of staphylococcus but its pathogenicity was not seriously investigated. Thus, Kraus, in 1900, first demonstrated the production of hæmolysin in blood-agar plates and Neisser and Wechsberg, in 1901, demonstrated its presence in culture filtrates. The presence of leucocidin was first demonstrated by Van de Veldee in 1904. Kraus and Pribram, in 1906, discovered the lethal action of staphylococcus filtrate in rabbits and Russ, in 1916, gave a more detailed account of the lethal toxin. Nicolle and Caseri, in 1914, first showed the necrotic action of the filtrate by subcutaneous injection. Walbum, in 1922, made an elaborate study on the toxin formation in a liquid medium and laid down the conditions necessary for

the production of such staphylo hæmolysin. Parker, in 1924, first introduced the method of injecting the toxin intracutaneously to produce necrosis in rabbits and later on, used an atmosphere of 10% of carbon dioxide during incubation of staphylococcal broth culture for the production of a good toxin. Bigger, Boland and O'Meara, in 1927, first demonstrated that a very potent toxin could be prepared by growing staphylococcus on the surface of agar instead of in a liquid medium as advanced by Walbum or Parker. The diverse actions of the so-called staphylococcus toxin, studied in fractions, by different workers, were not yet summed up and seriously considered to establish the true pathogenic action of staphylococcus pyogenes.

In 1928, there was a catastrophe at Bundaberg, in Australia, where 12 out of 21 children died as a result of the injection of a prophylactic diphtheria toxin-antitoxin mixture, found to be contaminated with staphylococcus pyogenes. That these contaminated staphylococci, now better known as "Bundaberg strain" might be the only factor responsible for the fatalities, was pointed out by the Royal Commission appointed under Dr. Kellaway to investigate into the cause of the disaster. This aroused a new interest in the study of the pathogenic action of staphylococcus pyogenes and stimulated a new research in the toxigenic and antigenic character of filtrates from staphylococcus cultures. A serious study on this micro-organism really began from this period. In addition to a series of work done by Burnet and others in Australia, bacteriologists from other parts of the world have also contributed massive literatures on research work done in different aspects, especially relating to its exotoxin, anatoxin and antitoxin. Now, in our present paper, we shall try to sum up in short these recent studies, dealing with some portions critically in the light of our own work, done in the B. I. Research Laboratory for the last few years.

Pathogenic Strains of Staphylococcus Pyogenes

Before we go into detail about the production of toxin by staphylococcus pyogenes, we shall first describe the following methods by which the nature of the true pathogenic strains of staphylococcus has been studied, such as, biochemical activities, growth in special media, antigenic structure, etc.

Formation of Pigment—From the point of pigment formation, Rosenbach (1884) divided the staphylococci into two classes, staphylococcus aureus and staphylococcus albus. Passet (1885) added a third variety, staphylococcus citreus with which we are not interested on account of its distinct lack of pathogenicity. Staphylococcus aureus is usually held to be more pathogenic than the albus ones but such estimation from the point of pigment formation may not be always correct. The formation of pigment depends on many variable factors and as such, it may not be always constant. Thus, a freshly isolated albus strain may develop yellow pigment after a few subcultures and an aureus strain, on prolonged subcultures, may lose its yellow pigment, sometimes not to develop again. Moreover, an aureus strain isolated from a single colony, after several generations, may produce, on plate cultures, colonies both of aureus strain and of albus variants. For example, the original "Wood" strain isolated by Burnet from a case of infected burns, was later on divided into two components Wood-86 (albus) and Wood-46 (aureus), both of which are equally pathogenic: Wood-86, the albus variant, has sometimes produced in our laboratory a more potent hæmolysin than the latter, showing that the pigment formation cannot be the decisive factor for its pathogenicity. Apart from pigment formation, other biochemical activities and serological reactions have been studied for the differentiation of staphylococcus aureus and albus but with no satisfactory result. Hence, all the pathogenic strains of staphylococci, whether aureus or albus, have, in this paper, been considered together as staphylococcus pyogenes.

Fermentation of Sugars—The fermentation of sugars by staphylococci is very variable. Generally, glucose, lactose, saccharose, maltose and mannitol are acted upon with the production of acid but not gas. Of these, mannitol and lactose are more important for differentiating pathogenic strains as these two sugars, especially the former, are very rarely attacked by non-pathogenic strains obtained from saprophytic sources. Mannitol is generally attacked by pathogenic strains very late, often after 48 to 72 hours.

Liquefaction of Gelatin—In liquefying gelatin, pathogenic strains are more active than the non-pathogenic ones and this property may be sometimes entirely absent in the latter.

Special Media for the Differentiation of the Pathogenic Staphylococcus—In isolating staphylococ-

cus pyogenes, it often becomes confusing to select the colony of the real pathogenic strain from the midst of those of the non-pathogenic ones growing together in the original agar culture, particularly when the material inoculated has got the chance of being contaminated with the latter. Of course, some virulent strains being highly hæmolytic, produce on primary culture in blood-agar media a clear zone of hæmolysis around the colony which is more marked, specially in the media prepared with rabbit's blood, though this may gradually become less apparent and ultimately absent on prolonged sub-cultures. With such a strain blood-agar media has really got some differentiating value but the difficulty remains the same with those that do not show any appreciable lytic zone in the primary culture in blood-agar media.

Chapman and Bernes (1935) advocated the use of a special media for the differentiation of staphylococcus pyogenes. This is a proteose-lactose agar containing crystal violet in a concentration of 1 in 300,000. A large inoculum is necessary for the growth of staphylococci in this medium which gives four kinds of colonies, (1) violet, (2) orange,(3) orange colonies with a violet fringe and (4) white colonies. As a rule, the first three kinds of colonies are formed by pathogenic strains while the white colonies are generally found to be of non-pathogenic ones. Chapman and others (1937) devised another similar medium in which bromthymol blue has been used instead of crystal violet, in a strength of 0·17 grm. per litre of proteose-lactose agar. In this medium, pathogenic staphylococci grow more easily and develop a characteristic bright golden yellow colour. The authors have claimed superiority of this medium over the former in the fact that it does not require a heavy inoculum for the growth like the former and also that the growth of most of the non-pathogenic staphylococci (nearly 94%) are completely inhibited in this medium. We have used both of these special media to make a study of their differentiating value and it is with bromthymol blue agar that we differ with the authors in often finding a free growth of non-pathogenic staphylococci with pale and white colonies without any change of colour, showing its complete inability to attack the sugar present in the media.

Antigenic Structure—Early workers attempted to classify staphylococci by means of simple agglutination tests with rabbit immune sera but the results have been uncertain and unreliable. Hine (1922) employed the more sure test of absorption of agglutinin and by this method, he was able to classify staphylococci into two main groups, staphylococcus pyogenes and staphylococcus epidermidis. Julianelle and Wieghard (1935) were able to isolate two different polysaccharides, one from pathogenic and the other from non-pathogenic strains, by means of chemical fractionation. These polysaccharides are non-antigenic in nature; but they give distinct precipitin reaction with the corresponding rabbit immune sera prepared against pathogenic and non-pathogenic strains. In preparing these sera, the vaccines are to be given intravenously for the development of anti-carbohydrate body. With such sera and those extracted polysaccharides, it is possible to determine the real nature of an unknown strain of staphylococcus. In actual tests, we have found that the precipitation is best obtained when the rabbit serum is used undiluted with a low dilution (1 in 20) of the homologous polysaccharide extract.

Staphylo-Coagulase—The fact that blood cultures from cases of staphylococcal septicæmia often show a loose fibrinous clot, led to the study of the coagulating substance formed by the staphylococcus. Loeb, in 1903, first described this phenomenon and Much in 1908 stressed its association with the pathogenic staphylococci. For its demonstration, a loopful of a 24-hour culture of a pathogenic strain is mixed with 0·5 c.c. of citrated human or rabbit plasma and after a few hours' incubation, the plasma becomes firmly clotted due to the action of the coagulase formed by the staphylococcus. Its presence in the culture filtrate can also be demonstrated in a similar way. The formation of coagulase being closely associated with the pathogenic strains and being very easily demonstrable, Cruickshank (1937) recommends its use as a routine test for determining the pathogenicity of the organism. Staphylo-coagulase is heat-stable and can resist temperature up to 100°C. for half an hour. It is non-antigenic as the serum of rabbits immunised with the culture-filtrate fails to inhibit the clotting property of the latter. In severe cases of staphylococcal infection, it is quite likely that the formation of this factor in the actual lesion is responsible for causing vascular thrombosis. Gengou (1933) regarded that though coagulation of plasma is the first

effect of coagulase, it is essentially a lytic substance, because, on further keeping the clotted plasma in the incubator, it again gets completely liquefied. Erwin Neter (1937) has made an elaborate study on the actions of the supernatant fluid of staphylococcal culture on human and rabbit plasma and has demonstrated the coagulating, anti-coagulating and fibrinolytic properties, possibly due to three different factors termed as (1) coagulase, (2) anticoagulant and (3) fibrinolysin. Of these, coagulase has just been described.

Anticoagulant—The actual existence of this factor has not yet been clearly understood. Neter himself remarks that, "because of the importance of carbohydrates for the development of anticoagulant, the question arises, whether or not the resulting acidity of the culture medium may be responsible for the inhibition of the plasma clotting". In any way, this anticoagulating property develops only in broth culture containing carbohydrates but not in plain infusion broth. Its presence can be demonstrated in the undiluted supernatant fluid of glucose broth cultures, which when mixed with human plasma, with the addition of calcium chloride and kept in the incubator for some time, is found to have inhibited the coagulation of the same plasma. This anticoagulating factor, though simultaneously present with the plasma-clotting factor in glucose broth cultures, can inhibit the action of the latter up to a certain strength but does not destroy it, as its presence becomes manifest again in dilution when the action of the former is no longer effective.

Fibrinolysin—Its presence has been demonstrated in the supernatant fluid of some pathogenic staphylococcus cultures which, when mixed with human plasma and kept in incubator, results in, at first clotting of the plasma and then in dissolution of the plasma clot. Staphylococcus fibrinolysin is effective towards human as well as animal plasma. That it is antigenic and can be specifically neutralised by an anti-serum, has been demonstrated by Neter with a serum obtained from a patient with chronic osteomyelitis. The plasma of the patient was shown to be resistant towards the action of staphylo-fibrinolysin whereas it was not so in the case of plasma obtained from normal individuals or from children with scarlet fever.

Pathogenicity—Hitherto we have tried to classify staphylococcus into pathogenic and non-pathogenic groups, mostly by means of *in vitro* methods. But the real pathogenic or non-pathogenic nature of a micro-organism is judged from the effect of its inoculation into susceptible lower animals. Most of the strains of staphylococci isolated from suppurative lesions or from blood cultures, are found to be more or less pathogenic for rabbits, mice, and to some extent for guinea-pigs. On the other hand, non-pathogenic strains obtained from saprophytic sources are harmless to these animals. The two important pathogenic weapons of staphylococcus are pyogenicity and toxicity. On subcutaneous injection of staphylococcus pyogenes into a laboratory animal, an inflammatory condition along with the mobilisation of polymorphonuclear cells takes place through the chemotactic influence of the cell bodies. A fighting process ensues against the defensive mechanism and as a result of the phagocytic action of the leucocytes, the cocci become arrested, partly destroyed and partly translocated by the time when they have already done some injury in causing destruction of the surrounding tissue cells and ultimately of the leucocytes themselves through the liberation of some toxic factors, necrotoxin, leucocidin, hæmolysin etc. This is just what happens in a localised staphylococcal infection such as boils, carbuncles etc. On intraperitoneal injection of a highly toxigenic strain into a rabbit, the animal usually dies as a result of acute septicæmia and toxæmia. This condition may sometimes develop even from subcutaneous or intradermal injection where the cocci are ultimately able to invade the bloodstream of the animal. This is what takes place in cases of acute staphylococcal septicæmia.

The virulence or toxicity of a highly pathogenic strain sometimes suddenly diminishes like strains of other virulent micro-organisms during maintenance in the laboratory. The real cause and nature of this sudden change cannot yet be exactly ascertained. Bigger (1933) has explained this to be due to the overgrowth of an inactive form already present in the culture. Lyons (1937) has demonstrated an encapsulated invasive phase of staphylococcus in diplococcal forms and it may be that the loss of virulence is due to the loss of capsules in the altered forms. Whatever may be the cause of such change, it is, however,

possible to raise the virulence and toxicity of such a strain by several repeated passage through rabbits or mice.

Culture Media for the Production of Toxin

Before we go into detail about the nature of the staphylococcal exotoxin, we shall first discuss about the composition of the various culture media and the conditions favourable for the formation of such toxin. Walbum (1922) used a liquid medium containing buffered broth with 0·5% of Witte peptone and 0·3% of magnesium sulphate and the reaction adjusted to about pH 7, the formation of toxin reaching its maximum within 3 to 4 days. Parker (1924) also used a liquid medium, a buffered broth containing proteose-peptone and used an atmosphere of 10% of carbon dioxide during incubation for the formation of a good toxin. Bigger, Boland and O'Meara (1927) advocated the use of agar in the medium for the preparation of a much more active toxin. By washing staphylococci off from the surface growth of such agar culture with saline and by centrifuging the suspension so obtained, they found the toxin (hæmolysin) present in the clear supernatant fluid. Burnet made an extensive study on staphylococcal exotoxin since the Bundaberg disaster in 1928 and he published a series of papers on the subject as a result of his serious investigation into the matter. In preparing exotoxin, Burnet (1929) at first used Parker's liquid medium in an atmosphere of 10% CO_2 but subsequently he (1931) adopted the method of growing the organism in agar media (0·8%) at pH 7·6, incubating the culture in an atmosphere of 20 to 30% of CO_2 for 24 hours and extracting the toxin from agar by means of saline. Later on, Burnet and Freeman (1932) used a semi-solid agar medium (0·3%) containing beef heart extract with 1% proteose-peptone at pH 7·2 and incubated for a period of 72 hours in an atmosphere of 25% of CO_2, 55% of O_2 and 20% of air. Burnet has shown that the use of sodium or calcium salts in Walbum's liquid medium is somewhat inhibitory to toxin formation while the presence of a trace of magnesium salt is essential for its production. He has also thoroughly discussed about the significance of using CO_2 for toxin production. With the growth of this bacteria, the medium turns to be gradually more alkaline but the toxin is best produced when the reaction of the mediums is maintained near about at pH 7. The reaction could be stabilised at this level by using sufficient phosphate buffers but such a high salt concentration in the medium has also been found to be inhibitory to toxin production. The function of the use of CO_2 is to act as a buffer, diminishing the progressive alkalisation of the medium during growth: besides, CO_2 or H_2CO_3 has the power to pass into the bacterial cell, thus increasing the intracellular acidity without the least damage to the cell. The use of agar either in solid or in "gel" form has been found to be distinctly superior to liquid medium but its function in influencing the toxin formation has not yet been clearly explained. Parish and Clark (1932), Dolman (1932-b) and other workers, since then, have followed Burnet's technique of growing staphylococcus in soft agar under excess of CO_2, either in its original or in a slightly modified form. Bigger, in 1933, again published a paper on the production of staphylococcal lysin and in this, he exhaustively dealt with the influence of different constituents of the medium in the formation of toxin. He used a buffered glycerol standard medium containing 0·5% glycerol in a buffered broth with the idea that, the addition of fermentable carbohydrate (glycerol) and phosphate buffer in this medium would eliminate the further use of CO_2 during incubation. By growing his particular strain "AY" as well as the "Wood" strain in this medium without the help of CO_2, he actually obtained a potent toxin in the saline extract of the agar culture. As already stated, staphylococcus tend to develop a highly alkaline reaction in the medium during growth but the simultaneous attack of staphylococcus on the carbohydrate causes an acid reaction and thus maintains the pH at a correct level. Bigger has shown that glycerol along with buffer salts serves the purpose better than when glycerol alone is used. He has also differed with Burnet in pointing out that the presence or absence of sodium or calcium and magnesium salts in this solid medium would be of little importance having no significant action over the formation of toxin. Leonard and Holm (1935) used a buffered semi-synthetic infusion-free medium as the base for a 0·3% semi-solid agar, the reaction adjusted to pH 7·4 and the culture incubated at 37° C. in an atmosphere of 20% of CO_2 and 80% of O_2, for 48 hours. Knight (1935) also has shown that staphylococcus can grow and form a toxin in a semi-synthetic medium. With the idea that

staphylococcus might grow and produce toxin on the small-molecule fraction of the routine media, Holt (1936) prepared a dialysed medium that is freed from large molecules through dialysis, with subsequent addition of powdered agar to a concentration of 0·6% and in such medium, staphylococcus actually formed a potent toxin. Douglas McClean (1937) has obtained toxin of adequate potency in a fluid "diffusate" from broth without the addition of agar. In preparing the "diffusate" medium, a dialysing apparatus has been employed, consisting of a cellophane bag containing sterile saline immersed in a broth medium, prepared after Bigger's method, the agar content only being omitted, allowing dialysis to take place overnight at room-temperature. According to McClean, it is not differential osmosis that influences staphylococcus to produce a potent toxin in a liquid medium but that cellophane acts as an adsorbing surface removing some unidentified substances already present in the broth which without affecting the growth of staphylococcus can inhibit the production of toxin. Previous workers have all maintained that the presence of agar in the medium, either in solid or in semi-solid form, markedly influences the formation of a good toxin but the true function of agar in such medium has not been clearly explained as yet. McClean points out that, like cellophane, agar acts as an adsorbing agent, removing from broth those unidentified substances inhibitory to the formation of toxin.

We have thus described, in short, the various culture media used by different workers for the preparation of toxin. We have scrutinisingly given trial of all those media more or less, but, for our routine production of toxin, we use either Burnet's or Bigger's medium in some modified form. The average yield of toxin in both these methods is quite satisfactory provided the strains of stock cultures are maintained in an ideal condition. The sudden fall in the toxicity of the stock strains can be avoided when these are preserved after the method of Swift (1937) in a "frozen and dried" condition. Highly toxigenic strains are selected for the production of toxin of average uniform potency, as with most of the pathogenic strains though freshly isolated, marked variations of their toxigenic power are observed though grown under the same condition in the same culture media.

Filtration of Toxin

The whole culture with agar is thoroughly agitated and filtered through paper or glass wool and then through a Seitz. E. K. filter. The pH of the filtrate should be near about 6·8 to 7 and if it is found to be at a much different level on either side, the pH of the toxin is immediately adjusted to the correct level, otherwise it may deteriorate very rapidly.

Properties of Staphylococcal Exotoxin

The toxin elaborated by staphylococcus in a fluid medium is a true exotoxin in nature. As will be shown later on, it has the power of giving rise to a potent antitoxin and it does follow the law of multiple proportion when combining with this antitoxin.

From a study of the various activities of this toxin, it is considered to be composed of the following principal antigenic factors in varying strength:

(I) Hæmolysin, (II) Necrotoxin, (III) Lethal toxin and (IV) Leucocidin.

1. *Staphylo-hæmolysin*—One of the various properties of the toxic filtrate of staphylococcus is to bring about hæmolysis of rabbit, sheep or human cells. The hæmolytic action on these different cells is due to different hæmolysins present in the filtrate. The hæmolytic action on rabbit cells was studied by various workers and specially by Burnet (1929). Bigger, Boland and O'Meara (1927) working with rabbit, sheep and human cells suggested the presence of different hæmolysins in the toxin; and Bigger (1933) first observed the "hot-cold" lysis with sheep cells. Glenny and Stevens (1935) at last showed that staphylo filtrates contain two antigenically different substances which they termed α-toxin and β-toxin. α-toxin hæmolyses both rabbit and sheep corpuscles at 37°C and the β-toxin hæmolyses sheep corpuscles only if incubation is followed by refrigeration (hot-cold lysis). The strains used by them produced either α-toxin alone or a mixture of varying amounts of α-and β-toxins. These findings were confirmed by Bryce and Rountree (1936) who were also able to produce pure β-toxin from strains isolated from bovine sources as already studied by Minett (1936). They used sheep's blood agar plates for the rapid determination of the type-toxin after the method of Naidu (1934) and they have shown that staphylococcus from human infection usually produce α-hæmolysin

while the majority of strains from bovine origin produce β-hæmolysin, though some strains, producing both types of hæmolysin may be found from human as well as bovine sources. The difference in action and nature of these α and β-toxin has been shown in a tabular form below.

	α-toxin.	β-toxin.
Rabbit cells.	Hæmolysis.	No Hæmolysis.
Sheep cells.	Lysis at 37°C.	Sometimes slight hæmolysis at 37°C. but rapid hæmolysis on cooling in the refrigerator (hot-cold lysis).
Intracutaneous injection into guinea-pigs and rabbits.	Necrosis.	No necrosis but flush in guinea pigs only.
Lethal action on rabbits and mice.	Yes.	No.
Action of formalin.	Easily changes to toxoid.	Sometimes proves more resistant to the detoxicating action of formalin.
Effect on heating.	Extremely heat-labile.	Destroyed by heat but a little more resistant than α toxin.
Antigenicity.	Yes.	Yes.

Morgan and Graydon (1936) further suggested the presence of two components in α-toxin, named as α_1 and α_2 toxin on the ground of their different combining power with antitoxin. Recently Roy (1937) has suggested the presence of human hæmolysin causing lysis of human as well as rabbit cells which is antigenically different from α-hæmolysin and probably identical with β-toxin of Glenny and Stevens though differing from the latter in causing the lysis of rabbit erythrocytes. Of these different hæmolytic factors, in staphylococcal toxin, just mentioned, the most important is the classical α-hæmolysin with which is closely associated the necrotising and lethal toxin.

II. Necrotising Toxin—Parker (1924) first used the intracutaneous method for the injection of staphylococcus toxin on rabbit. Burnet (1929) adopted this method in studying the necrotic action of staphylococcus filtrate and showed that 0·2 c.c. of toxin in certain dilutions gave well-marked skin reaction (necrosis) on rabbits and guinea-pigs. The intensity of skin reaction is judged by the size of the lesion and is best read on the second or third day. At first, thre is a superficial mottled area of necrosis in the centre of a white indurated patch with a definite rim of erythema but this gradually spreads deeper and downwards and on coalescing, a circular necrotic patch, dark in colour, appears over the area. (See Fig. No. 1.)

III. Staphylococcus "Killing Toxin"—On intravenous injection of staphylococcal toxin into rabbits, the animals die within a few minutes. The animal, after injection, appears normal up till a minute or two before its death when it suddenly develops some symptoms as stated by Burnet very exactly in the following lines: "the first sign is a certain unsteadiness, the rabbit falls over and shows rapid shallow breathing for some seconds; respiration then becomes irregular and gasping, sometimes the animal screams, incoordinate running movements occur and the corneal reflex is rapidly lost; respiration and all other muscular activities cease and at this stage evacuation of urine is common." According to Kellaway, Burnet and Williams (1930), the cause of the rapid death of the animal is due to an acute heart-failure following obstruction of the pulmonary circulation.

IV. Leucocidin—Staphylococcus filtrate has got destructive action on both human and rabbit leucocytes owing to the presence of a toxic substance known as leucocidin. This is extremely unstable, and the toxin loses the potency of this factor very rapidly. The leucocidin is capable of acting as an antigen giving rise to a specific antibody in the serum. By means of toxin treated with erythrocyte stroma and with leucocytes, Weld and Gunther (1931) showed that leucocidin was quite distinct from necrotising toxin. Panton and Valentine (1932) found a close

relation between the hæmolysin and necrotoxin but not with the leucocidin. According to Wright (1936) the leucocidin as determined with rabbit leucocytes by the Neisser-Wechsberg technique (N. W. leucocidin) was identical with *a*-hæmolysin and quite different from that shown by Panton and Valentine (P. V. leucocidin) which was tested in a different method with both human and rabbit polymorphonuclear leucocytes. Valentine (1936) and Proom (1937) cleared up this confusion by pointing out that *a*-toxin having some destructive action on rabbit leucocytes appeared identical with N. W. leucocidin. They described new methods for determining the existence of a true leucocidin having destructive action on both human and rabbit polymorphonuclear leucocytes but without any effect on their red cells. Valentine gave more importance to leucocidin than *a*-hæmolysin as the former facilitates the invasion of the tissue by destroying the phagocytic cells of the blood and as such, the value of antitoxic sera, in some cases, depends more on the anti-leucocidin than on the anti-hæmolysin content of the same.

FIG. NO. 1

Showing the necrotic action of staphylococcus toxin on the skin of a rabbit. 0·1 c.c. toxin of different dilutions, 1 in 100, 1 in 150, 1 in 200, 1 in 250, 1 in 300, 1 in 400 and 1 in 500 has been injected in order in different spaces from No. 1 to 7. Space No. 7 showing an area of necrosis of the desired size, the m.d.n.d. of the sample of toxin is 0·0002 c.c. In space No. 8, 0·1 c.c. of heated undiluted toxin has been injected and the toxin being destroyed by heat, gives no trace of reaction.

V. Staphylo-Enterotoxin—Certain strains of staphylococcus when grown under suitable condition, specially in a medium containing some starch, gives rise to a so-called enterotoxin which is filtrable and fairly thermostable. This substance has been responsible for a number of outbreaks of food poisoning. When taken by mouth, it has an intensely irritating effect on the gastro-intestinal mucosa. The nature of this toxin is uncertain but it is distinct from the hæmolytic, necrotising and lethal toxin and its antigenicity has not yet been established.

Of all these toxic factors just described, the *a*-hæmolysin, necrotising toxin and the lethal toxin are usually held more important in estimating the potency of a toxin. Since the work of Burnet (1929), this hæmolytic, dermonecrotic and phlebolethal properties of staphylococcus toxin are believed to be manifestations of a single antigenic substance on the grounds that, (1) there appears to be a fairly constant relationship between these three activities in different batches of toxin, (2) all these activities are destroyed at the same time when exposed to a temperature of 56°C for half an hour, and (3) an antiserum prepared against any given toxin invariably shows a specific and proportionate neutralising effect against all the three different activities of the toxin and moreover, (4) an antitoxin when titrated by any of the three methods—hæmolytic method with rabbit cells, intracutaneous method into guinea-pigs or by intravenous method into mice, gives approximately the same amount of titre. Of course, the unicity of this toxin is doubted when these different activities are not proportionately found in filtrates of some staphylococcus cultures. We have come across a strain "D. S. " giving high lethal toxin but negligible amount of hæmolysin and dermonecrotic toxin. We have also noticed a vari-

ant form of "Wood-46" strain, (after passage through mice for more than fifty times) which began to form a fairly potent dermonecrotic toxin (1500 m.d.n.d. per c.c.) but a very low amount of hæmolysin (20 m.h.d. per c.c.)

Titration of Toxin

Each lot of toxin before it is treated for conversion into toxoid and used for immunising purpose, is tested for its hæmolytic, dermonecrotic and lethal potency in the following way:—

1. *α-hæmolytic titre*—Dolman (1932) defines one minimal hæmolytic dose (m.h.d.) as the amount of toxin which will hæmolyse 1 c.c. of 1% suspension of rabbit R. B. C. in one hour at 37°C. A row of test tubes is set up in a rack and each receives 0·5 c.c. of increasing dilutions of toxin and 0·5 c.c. of a 2% rabbits cells suspension making a total volume of 1 c.c. in each tube. This is then incubated at 37°C for one hour and kept at laboratory temperature for one hour more when the reading is taken. The last tube showing complete hæmolysis gives the end-point. The titre of the toxin per c.c. is taken to be double the inverse of the toxin dilution from which 0·5 c.c. has been taken in that particular tube. For example, if the last tube showing complete hæmolysis be the one which received 0·5 c.c. of 1 in 1000 dilution, then the hæmolytic titre of the undiluted toxin would be 2000 m.h.d. per c.c.

2. *Dermonecrotic titre*—As defined by Dolman, the minimal dermonecrotic dose (m.h.n.d.) is the least amount of toxin which will induce on intradermal injection into the back of a closely clipped rabbit, an area of necrosis having a diameter of at least 0·5 cm. A healthy adult white rabbit (1½ to 2 kgms.) is taken. The back and sides are closely clipped and rubbed with a paste consisting of 50% barium sulphide and 50% starch and immediately washed well. Next day, 0·1 c.c. of different dilutions of the toxin is injected intradermally at different sites and the reactions are observed after 48 hours. The m.d.n.d. is taken as the least amount of toxin present in 0·1 c.c. of the diluted toxin causing a definite necrosis on the 2nd or 3rd day, the size of which is not less than 0·5 cm in diameter and the inverse of this is the dermonecrotic titre of the undiluted toxin per c.c. For example, if 0·1 c.c. of 1 in 300 dilution of toxin causes necrosis of the desired size, the m.d.n.d. of the particular toxin is 1/3000 c.c. and the dermonecrotic titre of the toxin would be 3000 m.d.n.d. per c.c. (Fig. No. 1).

3. *Minimal lethal dose (m.l.d.)*—The minimal lethal dose of the toxin is usually determined on rabbits of adult size and this is the least volume of toxin per kgm. weight of a normal rabbit which when given intravenously, will result in death within a few minutes. An average good toxin should have an m.l.d. of not more than 0·25 c.c. per kgm. body weight of the rabbit.

Staphylococcus Toxoid

Staphylococcal toxin of satisfactory potency is converted into toxoid or anatoxin by the addition of 0·3% formalin and keeping it in the incubator at 37°C for near about three weeks. Dolman and Kitching (1936) have suggested that toxoid must be prepared from toxin having the following minimum potency:

1. The minimal hæmolytic dose (m.h.d.) must not exceed 0·002 c.c.

2. The minimal dermonecrotic dose (m.d.n.d.) must not exceed 0·005 c.c.

3. The minimal lethal dose (m.l.d.) must not exceed 0·25 c.c. per kgm. weight of rabbits.

The average lots of our toxin at present used for conversion into toxoid show an m.h.d. of 0·001 c.c; m.d.n.d. of 0·0002 c.c. and an m.l.d. of 0·25 c.c. per kgm. body weight of rabbits.

Before using any lot of toxoid for immunising purpose, it is at first tested for its innocuity. According to Dolman, a toxoid for immunising purpose should satisfy the following points:

1. The undiluted toxoid must not cause any hæmolysis of 1 c.c. of 1% rabbit cells within 1 hour at 37°C.

2. 0·2 c.c. of the undiluted toxoid, when injected intradermally into a rabbit, must cause no necrosis.

3. 3 c.c. of the undiluted toxoid, per kgm. weight of rabbit, must have no lethal effect on intravenous injection into rabbits of average 2 kgm. weight, having less than 0·07 unit of antitoxin content in their serum.

4. 5 c.c. of the toxoid given subcutaneously into a guinea-pig or 0·5 c.c. given intraperitoneally into a mouse must cause no untoward effect.

ANTIGENICITY TESTS OF STAPHYLOCOCCUS TOXOID

The antigenic power of each lot of toxoid is always estimated before it is released for clinical use. This is done by several methods as have been dealt with in detail by Burnet (1931), Parish and Clark (1932), Dolman and Kitching (1935) and Leonard and Holm (1935).

1. Rabbit antigenic test—Dolman has adopted an arbitrary standard of minimum potency of a toxoid as such that if two weekly intravenous injection of 3 c.c. of toxoid per kilo weight of rabbit be given to a rabbit of 2 kgms. weight with a natural antitoxin of less than 0·07 unit, it should develop a circulating antitoxin of at least 0·5 to 1 international unit and should acquire a skin resistance of at least 20 m.d.n.d. doses of toxin.

The average supply of rabbits in our laboratory being less than 2 kgms. weight, we had to alter the doses. Three injections of 2 c.c., 4 c.c. and 4 c.c. are generally given at one week's interval, the last dose being given subcutaneously. The rabbits are bled on the 8th day for estimating the increased circulating antitoxin. We have frequently found that rabbits with a natural antitoxin of less than 0·05 unit per c.c. have finally shown 2 to 2½ units per c.c. in their blood after three injections of toxoid, prepared at different times during these experiments. We have also noted that the circulating antitoxin in these rabbits reaches its maximum near about the 14th day after the last injection. In titrating these sera of the immunised rabbits, a test dose of toxin determined against 0·1 unit of the standard antitoxin is generally used for convenience. The actual titration is done by the hæmolytic method which we shall describe in detail in connection with antitoxic sera prepared from horses.

2. Flocculation test for determination of Lf units—Burnet (1931) showed that a true toxin-antitoxin flocculation could be obtained in the case of staphylococcus similar to diphtheria and other toxin-antitoxin mixtures. The toxoid also gives the same flocculation as given by the original toxin with little variation. The flocculation test is done with each lot of toxoid using a fresh antitoxin of known strength and Lf unit of the toxoid is determined from the amount of antitoxin present in the tube which shows the flocculation first. This would be more clear from a particular test as given below:

Antitoxin No. 426 (100 units per c.c.)
Toxoid Lot No. 57.

Several tubes were set up in a rack and each received 1 c.c. of the toxoid. The antitoxin was diluted 1 in 2 and varying quantities from 0·1 to 0·5 c.c. was added in each tube by means of a Kahn pipette, the volume in each tube made up to equal quantity by means of saline. The rack was then placed in the water bath at 45°C. After one hour and a half, the tube, containing 0·3 c.c. amount of serum, first flocculated, as read by means of a lens. 0·3 c.c. of the diluted serum (1 in 2) contained 15 units and hence 1 c.c. of the toxoid (Lot. No. 57) contains 15 Lf units.

3. Antitoxin-binding test of toxoid for determination of Lb dose—This is determined by putting into a series of tubes, one unit of antitoxin and varying amounts of the toxoid under test over a suitable range. The mixtures are brought to a constant volume with saline and incubated at 37°C for one hour. Now 0·5 c.c. of 1 in 10 dilution of a toxin of a known Lh dose is added as "indicating dose" in each tube along with 0·5 c.c. of a 2% rabbit cell suspension. The tubes are well shaken and again incubated at 37°C for one hour. The tube which shows a 20% hæmolysis after one hour, contains a part of the Lh dose of toxin as well as some amount of toxoid which completes one full Lh dose, having binding power with one unit of antitoxin. Thus, from the Lh value of the toxin and from the amount of toxoid present in that particular tube, the binding unit (Lb dose) of the toxoid per c.c. is easily determined. Of course, the result determined by such methods may not be accurate on account of the influence of Danysz effect as recently discussed by Smith and Price (1938).

Regarding the last two in-vitro tests for the antigenicity of staphylo toxoid, Dolman has adopted a provisional standard maintaining that the toxoid should contain at least six flocculating units (Lf) per c.c. and at least five antitoxin-binding units (Lb) per c.c.

Holt (1936) has shown that staphylococcus toxoid can partially be purified by saturation with ammon. sulphate and then by dialysing the precipitated toxoid in running tap water for 2 to 3 days. The toxoid can also be purified by precipitating with trichlor acetic acid according to the method of Ramon (1936).

Clinical Use Of Toxoid

Staphylococcal toxoid is now widely used both as prophylactic against and treatment of staphylococcal infection such as recurring boils, carbuncles and other chronic staphylococcal skin diseases. Dolman (1935), Murray (1935), Connor (1935), Whitby (1935) and others gave an extensive clinical trial on patients suffering from various localised staphylococcal infection and all of them have independently obtained excellent results. In olden days, immunity in staphylococcal infection used to be considered as wholly antibacterial but recent researches have shown that it is mainly antitoxic and as such, the use of vaccine has been much replaced by toxoid. Kitching and Farell (1936), Downie (1937) and Smith (1937) have done animal experiments showing that vaccine is inferior to toxoid as immunising agent. Bigger (1937) in supporting the opinion of Dolman (1935) points out that the good results, sometimes obtained from vaccines prepared in the ordinary way, are probably due to the presence of some amount of toxin or toxoid formed along with the growth of cocci on solid media and carried into the saline emulsion in the form of vaccine. But still, he does not support the idea of abandoning the use of vaccines altogether as, in his opinion, to produce an effective immunity, both antibacterial and antitoxic bodies should be developed.

Antitoxin

For the production of staphylococcus antitoxic serum, horses are immunised against staphylococcus toxoid in gradually increasing doses more or less in a way similar to the production of diphtheria or tetanus anti-toxin. At the later stage of immunisation, fresh and untreated toxin may be used. By immunisation with plain toxoid, several horses have given a titre of average 250 units per c.c. At present we are trying to immunise several horses with alum precipitated toxoid as well as toxoid with tapioca, with the idea of getting a much higher titre but regarding the effect of these adjuvants, we cannot say anything definitely as yet.

Horses are sometimes immunised both against living emulsions of staphylococcus and the toxoid at the same time with the idea of developing in their blood both antibacterial and antitoxic bodies, but as serum in this form cannot be subjected to the process of concentration owing to the loss of its antibacterial bodies, massive doses would generally be required for the supply of necessary amount of antitoxin.

The antitoxin is almost entirely associated with the pseudo-globulin fraction of the serum. This can be concentrated according to the standard method by fractional precipitation with ammonium sulphate and by dialysis. The titre of the average lots of the concentrated sera, as done in this laboratory, has been found to be nearly four times the titre of the original sera.

Titration of Antitoxin

The antitoxin is titrated by any of the three methods as suggested by Hartley and Smith, in the Memorandum on a Provisional Stable Standard for Staphylo Antitoxin. The standard antitoxin containing 20 International units per c.c. as supplied by the League of Nations, and a suitable test toxin in a somewhat stable condition are used in the titration of these antitoxins. The test toxin used for titration should be such as would (1) cause the hæmolysis of rabbit R. B. C. in doses of 0·005 c.c. or less, having a test dose (Lh) of 0·3 c.c. or less, (2) produce a small characteristic necrotic lesion in guinea-pigs when injected intracutaneously in doses of 0·01 c.c. or less and having a test dose (Lr/5) of 0·1 c.c. or less, (3) be lethal for mice when injected intravenously or intraperitoneally in doses of 0·05 c.c. or less, having a test dose (L+) of 0·3 c.c. or less.

The test toxin may better be preserved in the refrigerator in a concentrated and dried condition as is usually done in cases of other unsuitable toxins.

A. Titration by Hæmolytic Method:

(1) Determination of the test dose (Lh) of toxin.

In a series of tubes, 1 c.c. of the dilution of the standard antitoxin containing 1 unit is taken. A varying quantity of the test toxin in a suitable dilution is added and the total volume of each tube is made up to 2 c.c. with saline. The tubes are then allowed to keep at room temperature for 30 minutes. Then 0·5 c.c. of a 2% rabbit R. B. C. suspension is added and the rack is placed in the incubator at 37°C for 1 hour. The tubes are then left at room temperature for one hour more and the reading is then taken. The test dose (Lh) of the toxin is the amount present in 2 c.c. of that mixture which shows a partial hæmolysis of rabbit R. B. C. added as indicator.

(2) Titration Proper. The test toxin is diluted in such a way that 1 c.c. contains the test dose (Lh). Now 1c.c. of this diluted toxin is taken into each of a series of tubes to which is added different quantities of antitoxin in suitable dilution. Another tube also receives 1 c.c. of the diluted toxin and 1 unit of standard antitoxin. The total volume of each mixture is adjusted to 2 c.c. with saline. The tubes are kept in the room temperature for 30 min. and then 0·5 c.c. of a 2% rabbit R. B. C. suspension is added in each tube. The mixtures are incubated at 37°C for one hour and then left at room temperature for another hour. The reading is now taken. The amount of antitoxin present in the mixture of the tube showing the same or near about the same degree of hæmolysis as shown by the mixture containing 1 unit of standard antitoxin, is equal to 1 unit of antitoxin and from this, the potency of the diluted antitoxin is calculated.

B. Titration by Intracutaneous Method on Guinea-Pigs.

(1) Determination of test dose Lr/5.

The standard antitoxin is diluted in such a way that 1 c.c. contains 2 units of antitoxin. 1 c.c. of this

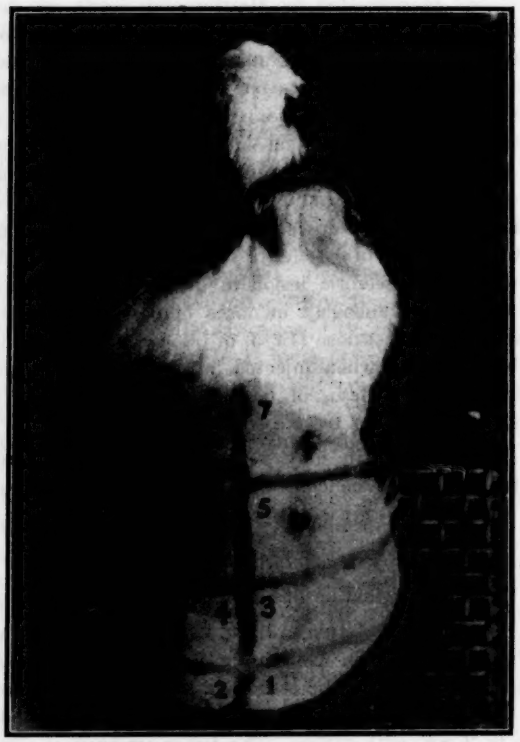

FIG. No. 2

Showing the skin reactions on a guinea-pig in determining the test dose Lr/5 of toxin lot. No. 39. 0·2 c.c. of the mixtures injected in spaces Nos. 1 to 4, containing less amount of toxin than the test dose, gives no reaction. Space No. 5 shows the desired reaction while Nos. 6, 7 and 8 show larger area of necrosis due to the presence of greater amount of toxin than the test dose.

FIG. No. 3

Showing the skin reactions on a guinea-pig in the actual titration of an antitoxin, No. 516 (con) by the intracutaneous method. Space No. 6 shows the reaction given by the test dose Lr/5. Space No. 3 shows nearly the same degree of necrosis as given by the test dose Lr/5 in Space No. 6. Spaces No. 1 and 2 showing either no reaction or a smaller area of necrosis and spaces No. 4 and 5 showing larger area of necrosis according as the antitoxin present in 0·2 c.c. of the mixtures injected is greater or lesser than 0·2 unit as present in the test dose Lr/5.

diluted antitoxin is taken into each of a series of test tubes to which is added a varying quantity of toxin in a suitable dilution and the total volume in each tube is made up to 2 c.c. with saline. These are allowed to stand at room temperature for half an hour. 0·2 c.c. of each mixture is then injected into the depilated skin of at least two white guineapigs weighing 300 to 400 grms. Th skin reactions are seen after 24 to 48 hours. The test dose Lr/5 of the toxin is that amount present in 0·2 c.c. of the mixture which causes a small but characteristic necrotic lesion in the skin of the guinea-pigs. (*vide* Fig. No. 2).

(2) Titration of antitoxin. The test toxin is diluted in such a way that 1 c.c. contains 10 times the test dose Lr/5. 1 c.c. of this diluted toxin is taken into each of a series of test tubes containing different quantities of antitoxin in suitable dilution. Into a separate tube, 1 c.c. of the diluted toxin is added with 1 c.c. of the diluted standard antitoxin containing 2 units per c.c. The tubes are allowed to stand at room temperature for 30 min. An amount of 0·2 c.c. of each mixture is injected at suitably spaced intervals into the depilated skin of two white guinea-pigs of 300 to 400 grms. weight. The reactions are observed after 24 to 48 hours. The mixture from which 0·2 c.c. causes the same degree of necrosis as that produced by 0·2 c.c. of the mixture containing standard antitoxin shows that it contains 0·2 units in 0·2 c.c. of the diluted antitoxin from which the titre per c.c. is easily calculated. (*vide* Fig. No. 3).

C. Titration by Intravenous Injection Into Mice:

(1) The test dose (L+) is determined in the following way:—

Into a series of tubes mixtures are made in such a way that 0·5. c.c. of each mixture contains 1 unit of the standard preparation in a suitable volume and a varying quantity of toxin in suitable dilution. The total volume of each mixture is made up to 0·5 c.c. by means of saline. The mixtures are allowed to stand at room temperature for 30 min. For each mixture, a group of 6 mice of 17 to 22 grms. weight are taken and 0·5 c.c. of the mixture is injected into the tail vein of each of those six mice. The other mixtures are also injected in the same way. The mice are observed for three days. The test dose (L+) would be that amount of toxin present in 0·5 c.c. of the mixture which causes the death of about 50% of the total number of mice injected with it.

(2) Titration of antitoxin. Different mixtures are made in such a way that 0·5 c.c. of each contains the test dose (L+) of toxin and a varying amount of antitoxin under test in suitable dilution. A separate mixture with the test dose and one unit of standard antitoxin is also made in a total volume of 0·5 c.c. The mixtures are allowed to stand at room temperature for 30 min. 0·5 c.c. of each mixture is injected into the tail vein of each of six mice of 17 to 22 gms. weight. The mice are observed for three days. The mixture which causes the death of the same number or very nearly the same number of mice as the mixture containing 1 unit of standard preparation, does actually contain an amount of serum equal to 1 unit of antitoxin, and from this, the potency of the antitoxin is calculated.

The actual titration of a particular antitoxin (concentrated), prepared in this laboratory, by the hæmolytic method and also by intracutaneous method on guinea-pigs, has been shown in the Tables No. 1 (a, b) and No. 2 (a, b) respectively. The antitoxin can also be titrated by intracutaneous method on rabbits or by intraperitoneal injection into mice in a similar way but the above three methods are usually followed. Titration of an antitoxin by any of these methods gives approximately the same result. Of these,the hæmolytic method is more commonly used as it has got several advantages over the other methods. An accurate result is obtained by this inexpensive method very easily and quickly, without the use of animals. Timmerman (1937) has raised the question that the test dose of a staphylococcus toxin determined by the hæmolytic method may be influenced by the individual nature of the cells of a rabbit used in the experiment and hence, suggests that the R. B. C. from the same rabbit which has been used in finding out the test dose (Lh) of the toxin, should also be used when assaying an antitoxin by the hæmolytic method. We have used emulsions of R. B. C. from different rabbits separately at a time, some of these even already immunised with toxoid, but the test dose (Lh) has been found to be almost the same without any significant variation in any case. The variation, if any, may be rather attributed to the slight variation in the strength of the different suspension of R. B. C. used in different experiments which, perhaps, is unavoidable to a certain extent. Llewellyn Smith (1937) has shown that glycerol in-

hibits the necrotic action of staphylococcal toxin and hence, when staphylococcal antitoxin is titrated by the intracutaneous method, the results sometimes differ from that found out by the hæmolytic method which is claimed to be due to the use of standard antitoxin containing glycerol as diluent.

Clinical Use Of Staphylococcus Antitoxin

Staphylococcus antitoxin being comparatively a recent addition to the list of antitoxic sera, much information regarding the results of its therapeutic use is not yet available. From the laboratory experiments, it has been shown that the antitoxin has got

Table 1 (a)

DETERMINATION OF THE TEST DOSE (Lh) OF TOXIN LOT. NO. 39.

	1	2	3	4	5	6	7	8
Standard antitoxin (diluted to contain 1 unit per c.c.)	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.
Toxin, Lot. No. 39 (in vol. of 1 c.c.)	0·02	0·03	0·04	0·05	0·06	0·07	0·08	0·09
2% rabbit R. B. C. suspension (added after half an hour at room temperature)	0·5	0·5	0·5	0·5	0·5	0·5	0·5	0·5
Hæmolysis (after one hour at 37°C. and one hour in room temperature)	–	–	–	–	+	+++	+++	+++

– = no hæmolysis. ++ = partial hæmolysis.
+ = trace of hæmolysis. +++ = complete hæmolysis.

Tube No. 5. showed very faint hæmolysis after two hours. From the above results, Lh. dose seemed to be a little higher than 0·06 c.c. but less than 0·07 c.c. To determine the exact test dose, another similar test, with toxin ranging from 0·06 to 0·07 by smaller increase in amount, was done and a correct test dose was found to be 0·062 c.c.

Table 1 (b)

ASSAY OF ANTITOXIN NO. 516 (CON.) BY THE HÆMOLYTIC METHOD.

	1	2	3	4	5	6	7	8	9
Test toxin, Lot. No. 39 (diluted so that 1 c.c. contains 0·062 c.c. of toxin)	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.
Standard antitoxin (1 c.c. containing 1 unit)	...	...	...	...	...	...	...	...	1 c.c.
Antitoxin No. 516 (con.)	1 c.c. (1:500)	1 c.c. (1:550)	1 c.c. (1:600)	1 c.c. (1:650)	1 c.c. (1:700)	1 c.c. (1:750)	1 c.c. (1:800)	1 c.c. (1:850)	...
2% rabbit R.B.C. suspension (added after half an hour at room temperature)	0·5	0·5	0·5	0·5	0·5	0·5	0·5	0·5	0·5
Hæmolysis (read after one hour at 37°C. and one hour at room temperature)	–	–	–	–	–	+	++	+++	++

– = no hæmolysis. ++ = partial hæmolysis.
+ = trace of hæmolysis. +++ = complete hæmolysis.

Tube No. 7 showing the same degree of hæmolysis as the control tube No. 9, the estimated potency of antitoxin No. 516 (con.) would be 800 International units.

TABLE 2 (a)

DETERMINATION OF THE TEST DOSE Lr/5 OF TOXIN NO. 39.

	1	2	3	4	5	6	7	8
Standard antitoxin (1 c.c. containing 2 units.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.
Toxin, Lot. No. 39 (in vol. of 1 c.c.)	0·05	0·1	0·15	0·2	0·25	0·3	0·35	0·4
After half an hour at room temperature, 0·2 c.c. of each mixture was injected intracutaneously into two guinea-pigs and reactions were observed after 48 hours.								
Guinea-pig No. 1 (weighing 390 grms.)	–	–	–	=	slightly less than ½ cm.	¾ cm.	¾ cm.	1½ cm.
Guinea-pig No. 2 (weighing 370 grms.)	–	–	–	=	½ cm.	1 cm.	1½ cm.	1½ cm.

– = no reaction.

Positive reactions have been metioned in the length of the diameter of the necrotic area.

In the above experiment, guinea-pig No. 1 with its skin reactions has been shown in fig. No. 2. The two guinea-pigs showing markedly varying reactions, the experiment was repeated with two other fresh guinea-pigs with the toxin ranging from 0·2 to 0·3 c.c., the difference of each tube being taken in 0·02 c.c. amount only and from this second experiment, the test dose Lr/5 was found to be 0·028 c.c. which was actually taken in the assay of the antitoxin.

TABLE 2 (b)

ASSAY OF ANTITOXIN NO. 516 (CON.) BY INTRACUTANEOUS METHOD ON GUINEA-PIGS.

	1	2	3	4	5	6
Test toxin, Lot No. 39 (diluted so that 1 c.c. contains 0·28 c.c.)	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.	1 c.c.
Standard antitoxin (1 c.c. containing 2 units).	...	...	...	...	...	1 c.c.
Antitoxin, No. 516 (con.)	1 c.c. (1:300)	1 c.c. (1:350)	1 c.c. (1:400)	1 c.c. (1:450)	1 c.c. (1:500)	...
After half an hour at room temperature, 0·2 c.c. of each mixture was injected into each of two guinea-pigs and the reactions were observed after 48 hours.						
Guinea-pig No. 1 (weighing 370 grms.)	–	less than ½ cm.	slightly more than ½ cm.	1 cm.	1½ cm.	½ cm.
Guinea-pig No. 2 (weighing 380 grms.)	–	less than ½ cm.	½ cm.	less than 1 cm.	less than 1½ cm.	½ cm.

In the above experiment, 0·2 c.c. of the mixture from tube No. 3 gave nearly the same degree of reaction as that given by the Lr/5 dose in the tube No. 6. Therefore, 1 c.c. of 1 in 400 dilution of the antitoxin present in the tube No. 3. being equal to 2 units, the potency of ths antitoxin No. 516 (con.) would be 800 International units.

The reactions in guinea-pig No. 1 of the above experiment has been shown in fig. No. 3.

an effective neutralising action on all the different activities of the toxin so far observed; and from this fact, it may be reasonably expected to be an useful agent in the treatment of acute local or generalised staphylococcal infections specially when accompanied with toxæmia or septicæmia. Formerly, a pure antibacterial serum was given a fair trial but with very unsatisfactory result. Recently, with staphylococcus antitoxin some favourable results have, of course, been already reported but, on further evidence on its more extensive clinical use, the exact value of this antitoxin will be assessed.

Before we conclude this paper, we must take this opportunity to offer our best thanks to the authorities of Bengal Immunity Company Ltd., for placing at our disposal ample facilities in undertaking the work on staphylococcus in various directions which will be separately published in more detail in subsequent papers. Our heartiest thanks are also due to Dr. S. P. Dey and Dr. P. N. Basu for their constant encouragement and valuable suggestions and also to Drs. B. Das and S. M. Biswas for their able and continued assistance in successfully carrying on the various experiments in connection with this new line of work. Lastly, we must thank Mr. B. Kar for kindly taking the excellent photographs of the animals shown in this paper.

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HISTIDINE AND PEPTIC ULCER

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Introduction

During digestion the ingested proteins escape, to a large extent, the peptic hydrolysis but liberate rapidly the amino-acids on coming in contact with trypsin. But different amino-acids are liberated at different rates either because some amino-acids occupy a more exposed position in the protein molecule than others or because certain amino-acids linkages are more readily hydrolysed than others; *e.g.* in a tryptic hydrolysate, histidine and other amino-acids appear in traces whereas tyrosin and cystin appear in larger quantities. But at a later stage of the digestion histidine does separate. Some portion of it is absorbed as such and some in a modified form, because normal bacteria in the gut decolorise or deaminase the amino-acids. In an acid medium, histidine is changed to histamine, but in a buffered or alkaline medium, histidine is either not catabolised or it is catabolised with the production of components not containing the imidazole ring. (Hanke and Koessler, 1924).

That histidine is an amino-acid essential to the body is evident from the fact that the hemoglobin of the red blood corpuscle contains 10% nearly of the amino-acid. But whether the amino-acid as such exists in the tissues or not is a much-debated question. Though Abderhalden (1922), Rose and Cox (1924), and Rose and Cook (1925) doubt, it seems to be established by individual elimination of amino-acids in feeding experiments by Ackroyd and Hopkins (1916) that the amino-acids arginin and histidine are interconvertible in the animal body and that either one is an essential constituent of a complete amino-acid mixture in a nutritional sense. And after absorption, it is also known that the amino-acids cannot be stored as such in the animal body, except in minute quantities as shown by Louis Leiter (1925)—' Intravenous injection of histidine hydrochloride causes a sharp rise in blood histidine (normally zero as estimated as histidine) with a rapid fall so that at the end of two hours only a few milligrams are present . . . Histidine was almost completely metabolised even after the injection of large doses and in the prsence of a high concentration in the blood.'

Aron (1933) propounded the theory that peptic ulcers form as a result of deficiency or deficient absorption of histidine. The experimental basis of his thesis was as follows:—Isolating the duodenum, deviation of the duodenal juice (after Mann and Williamson) into the terminal ileum, and establishing the continuity of the stomach with the cut end of the jejunum, invariably gave rise to peptic ulcers at the junction of the later anastomosis. Contending that the ulcer formation was due to deficient absorption of the products of protein metabolism due to elimination of the duodenum from the circuit, various amino-acids were injected in turn and it was claimed that the repeated injections of histidine healed up the ulcers. On the basis of these findings on experimental animals, Aron treated human beings suffering from peptic ulcer with histidine and observed beneficial results.

The exact way in which histidine acts is not known but various theories have been propounded.

Kean (1936) opines that normally there is a parallelism between the amount of acid and of the imidazole derivatives found in the gastric juice. In peptic ulcer this parallelism is disturbed, the concentration of imidazole bodies being lower than in normal individuals. Histidine is supposed to be broken by the liver histidase and thus the parallelism established.

Prof. Sir C. Stanton Hicks of the University of Adelaide (1937) observes that the injection of one ampoule of Larostidin Roche (a brand of histidine), rapidly increases the coagulaton rate of the blood to about 50% of its original value and suggests that it may play a considerable part in the initiation of symptomatic improvement of peptic ulceration.

Some others believe that histidine acts only psychically as, the suggestion of a new 'cure' by in-

jection relieves the patient of the subjective symptoms. Many have tried injecting bland solutions, the patient being kept on false ground that he is receiving histidine. Only two authors are quoted for brevity. Flood and Mullins (1936) gave a series of normal saline injections in eighteen patients and observed beneficial effects. Sandweiss (1936) also tried similarly in twenty cases and obtained successful results in an equal number of patients as with histidine.

Subsequent to Aron's postulation of histidine theory in 1933 an extensive clinical trial of the substance has been given all over the world. Of the innumerable favourable reports that have been appearing in the medical press corroborating Aron's views, only a few that have dealt with a large number of cases are referred to hereunder. Bulmer (1934, 1936)—52 cases; Kahler and Duregger (1936)—40 cases; David Smith (1935)—12 cases; Hessel (1935)—22 cases; Kean (1936)—33 cases; Symon and Nemec (1937)—9 cases; Winter (1937)—28 cases; Bogendoerfer (1936)—30 cases; Raftsky (1935)—24 cases; Eads (1936)—35 cases. And amongst those that had very good results with histidine were Lavastine (1936), Winter (1937) and McCurich.

Histidine was found to be of use not only in cases of peptic ulcer but also in ulcerative colitis, bronchiectasis, and small pulmonary abscesses, allergy with recurring headache, vertigo, bronchial asthma, with or without gastric symptoms. (Weston Oakes—1937).

The present report is the result of investigation of the therapeutic effect of histidine in peptic ulcer in a series of 16 cases. The cases that have been selected were such that medical treatment was definitely indicated; chronic cases with marked pyloric stenosis and obstruction, which necessitated only operative treatment were avoided. In each of the cases the following is the routine adopted.

Gastric analysis and barium meal and x-ray are done before treatment. The actual treatment comprising on an average, 21 to 25 daily intramuscular histidine injections of 5 c.c. of 4% histidine monohydrochloride. No other concurrent treatment was adopted. Many of the patients were hospitalized and no more diet than the hospital diet were allowed for them. The stool was examined twice a week for detection of occult blood. The patient was weighed weekly as well as before and after the treatment. The non-hospitalized patients were permitted to follow their normal avocations; nor was their diet restricted. Barium meal and x-ray were repeated in many and gastric analysis done in all the cases at the end of the treatment. Many of the cases were followed up-to date, *i.e.* for about one year after the treatment. The histidine solution used was that perpared by two renowned Western companies and the concentration and the reliability of the drug may be taken to be authentic.

The results are best described as short individual case notes.

CASE NOTES

Case No. 1.—K. S., male, 30 years old was admitted for the treatment of abdominal pain of two years' duration. History of occasional vomiting with relief of symptoms. The test meal analysis revealed a slightly high acidity in the one hour specimen after the gruel and blood throughout the first hour after the gruel. Occult blood was present in the stools. The barium meal was rapidly hurried through the stomach and duodenum and hence no details regarding the duodenal cap could be made out. The diagnosis of active peptic ulcer was made and the histidine therapy instituted. After the full course of 25 injections, there was no difference in the x-ray picture. The test meal showed no blood and the pain got better. The patient put on a weight of 7 lbs.

Case No. 2.—S. R., male, 24 years old came for the treatment of recurrence of epigastric pain of two months' duration. The pain used to appear during the first hour after the food. No vomiting. Gastric analysis showed moderate hyperacidity. Barium meal and subsequent x-ray showed definite defective filling of duodenal cap. There was no occult blood in the motion. A complete course of histidine was given. There was no difference in the gastric analysis, but the barium meal and x-ray showed a definite well filling duodenal cap. A follow up of the case showed that the patient was still having the pain till November, 1937.

Case No. 3.—B. K., a male labourer of 20 was admitted on 11-7-36 for regularly intermittent epigastric pain of one and half year's duration. Barium meal showed no abnormality in the stomach or duodenum, and a long segmented retrocæcal appendix. Test meal revealed no abnormality. Stool showed occult blood. While doing appendicectomy a non-indurated duodenal ulcer scar was noticed. As the removed appendix looked normal on histological examination and on the evidence of history and occult blood in motion, 22 injections of histidine were given. The test meal analysis during and after treatment showed no difference from the initial; nor the barium meal. Dyspeptic symptoms subsided with the 17th injection, but occult blood was present in motion even at the time of discharge. There was no recurrence of pain.

Case No. 4.—B. M., a convict of 32 years was admitted on 14-7-36 for the treatment of regularly intermittent epi-

gastric pain of four months' duration. Pain was relieved by vomiting, which never contained blood. On palpation the duodenal point was tender. Test meal showed a rapidly emptying stomach with reflex hyperacidity. Stool showed occult blood. Barium meal showed a continuous spasm of the stomach at about the middle. At operation a subacutely inflamed appendix was removed but no evidence of peptic ulcer was found. But the symptoms did not completely subside and on the basis of the occult blood in motion, x-ray findings and recurrence of symptoms after operation, a course of eleven histidine injections were given in the hospital and the remaining in the Central Jail. The x-ray picture showed the same appearance even after treatment and after about six months was again admitted with typical ulcer symptoms.

Case No. 5.—B. S., an undernourished male of West Godavari district aged 30 was admitted on 13-7-36 for the treatment of frequent epigastric pain of two months' duration. The pain was said to have commenced after an attack of post-pyrexial dyspepsia. Vague upper abdominal tenderness and rigidity of the upper recti were found on physical examination. Test meal showed a markedly hyperacid and hypermotile stomach. Barium meal and x-ray showed no abnormality in the gastrointestinal tract except for a long and segmented appendix, which was removed on 30-7-36 and was found to be a catarrhal appendix. At operation a hyperæmic patch on the lesser curvature of the stomach suggestive of an acute gastric ulcer was found. This operation finding with the persistence of the gastric hyperacidity and occult blood in the stool suggested a diagnosis of an early gastric ulcer and histidine treatment was instituted during the convalescence after operation. Total injections given were eighteen. The occult blood in the stool disappeared in the second week and a follow-up of the case for one year showed no recurrence of symptoms.

Case No. 6.—B. R., admitted on 4-7-36 for severe continuous abdominal pain aggravated with food within an hour and relieved by vomiting. He was rapidly losing weight. Incidentally he was found to have bilateral tuberculosis of the lungs and tubercular treatment instituted. Barium meal and x-ray showed rapid emptying of the stomach and a residual barium in the lesser curvature in the 3 hour 30 min. and 4 hour 45 min. pictures. Test meal analysis showed complete achylia and marked hypermotility of the stomach. The stool showed occult blood. A diagnosis of gastric ulcer (tubercular) was made and histidine treatment instituted. By the 14th injection the acuteness of the pain disappeared giving rise to a constant dull pain which did not disappear even on the 25th injection. After an interval of two weeks a second course of histidine was commenced. The patient had acute exacerbation of symptoms once just before the commencement and again during the second course. The patient in despair got himself discharged from the hospital after ten injections in the second course.

Case No. 7.—K. G., a male of 22 was admitted on 11-8-36 for treatment of severe epigastric pain of five years' duration, arising two to three hours after food and present for 1½ to 2 hours. Barium meal and test meal examinations showed no abnormality. There was no evidence of pyloric stenosis. Stool showed occult blood. The patient was given a full course of histidine treatment as an outpatient. After the seventh injection the acuteness of the pain disappeared and the occult blood by the 15th. But the patient got a bad relapse on the 16th day. At the end of the treatment x-ray showed an ill-formed duodenal cap and a positive occult blood in motion. The patient was readmitted and given alkaline treatment. A letter from the patient subsequently in August 1937, disclosed that the symptoms were still recurring. The post-treatment gastric analysis showed a definite increase in acidity than the pre-treatment analysis.

Case No. 8.—A. G., male of 30 was admitted for recurrence of pain since four months after an operation of gastrojejunostomy done in 1931. The pain was continuous, aggravated with food and relieved by vomiting. The stool contained occult blood. Test meal showed a marked initial hyperacidity and hypermotility. Blood was found in all the specimens. Barium meal and x-ray showed a well functioning stomach. On the basis of these findings the diagnosis of a jejunal ulcer was made and histidine treatment commenced. After the first injection there was a severe reaction, the temperature running up to 104°F. The treatment was temporarily stopped for four days and recommenced. Pain completely stopped by the 9th injection. But on the thirteenth day the gastric analysis still revealed a marked hyperacidity with blood in the latter two specimens. After the sixteenth injection the test meal analysis showed the acidity within normal limits and there was no occult blood either in gastric contents or in the motion. Follow-up could not be done.

Case No. 9.—P. S., was admitted on 18-9-36, with the history of irregularly intermittent epigastric pain of four years' duration, relieved by vomiting, voluntary or involuntary. Stool showed occult blood. Barium meal showed normal emptying time, the test meal showed a marked hyperacidity. The patient was given a course of histidine treatment as an out-patient. After one week the pain subsided only to recur in all its severity in the third week, which necessitated supplementing with alkalies. The occult blood was present even after the course of treatment, but there was a definite reduction in acidity as judged by the test meal. During the treatment the patient put on a weight of 8 lbs.

Case No. 10.—D. G., a lawyer from Vizianagram was given a course of histidine as an out-patient. He gave a familial history of the gastric trouble and a history of abdominal pain since five years, commencing three to four hours after food. Previously the patient was given alkaline treatment in the hospital without any effect. There was no occult blood in the stool. The barium meal showed a markedly deformed duodenal cap with a normally emptying stomach. The test meal showed a moderate hyperacidity. The effect of the treatment was that the painless intervals were longer. The subsequent test meal showed a slight increase in acidity and there was no increase in weight. In October, 1937, the patient was still having the attacks of pain and sought admission again into the hospital.

Case No. 11.—S. S., an ill-nourished Mahomedan young man was operated for chronic duodenal ulcer on 12-7-34 and a posterior no loop gastrojejunostomy and appendicectomy performed. Since August, 1936, intense agonising pain recurred, arising within half an hour after food and relieved by vomit which did not contain blood. Both test meal and barium meal revealed a well functioning stomach with free regurgitation of bile. Stool showed occult blood. After a complete course of histidine treatment, the patient completely improved as regards the vomiting but the pain was as severe as ever and hence the histidine treatment had to be supplemented with alkaline powders at the sixteenth day of treatment, after which there was a slight relief of pain. The occult blood was still present at the end of the treatment.

Case No. 12.—K. Th., a middle aged fisherman from Parlakimidi Taluk was operated on 4-6-36 for duodenal ulcer but seeing no actual duodenal ulcer the unhealthy looking chronically inflamed appendix was removed and the patient discharged. Subsequently the patient had attacks of abdominal colic twice and frequent dull pain at the same spot, where he was having the pain before. Afraid of recurrence patient sought admission again. On test meal examination it was noticed that there was marked initial hyperacidity and a subsequent marked rise. X-ray showed no definition of the duodenal cap and a stomach emptying in 5 hours. On the above findings a diagnosis of duodenal ulcer was made and the patient started on histidine treatment. After the complete course of treatment there was no recurrence of pain, but the post-treatment gastric analysis showed an acidity far higher than before. At the time of discharging the patient was complaining only of hyperacidity. A letter from him in October states that pain recurred after he left the hospital.

Case No. 13.—K. S., male, 24 years old was admitted for the treatment of severe daily abdominal pain of one and a half year's duration. Markedly dyspeptic: pain aggravated with food, was relieved by voluntary vomiting occasionally containing blood. Stool showed occult blood. Barium meal and x-ray showed an ill-formed duodenal cap. Test meal showed total and free acid within normal limits but abnormally high total chlorides in the resting juice: 125 c.c. N/10 per 200 c.c. On the basis of the above findings, a diagnosis of duodenal ulcer was made and histidine instituted. Post treatment gastric analysis showed a marked increase in acidity. At the end of treatment patient still complained of an occasional pain. Occult blood was present in the stool. The test meal showed definite increase in acidity.

Case No. 14.—R., male of 16 years was admitted for the treatment of abdominal pain of two years' duration. He had no vomiting but complained of constant acid eructations. Fractional test meal showed a marked initial acidity and reflex hyperacidity. Stool showed no occult blood. Barium meal and x-ray showed a normal emptying stomach and a deformed duodenal cap. The diagnosis of an active duodenal ulcer was made and the histidine treatment was instituted. The patient after the treatment felt complete relief from pain but the dyspeptic symptoms persisted. Occult blood was found in the motion at the time of discharge.

Case No. 15.—B. Y., a woman 36 years old was admitted with typical history of gastric trouble of six months' duration. The barium meal and x-ray showed a definite niche in the lesser curvature. The patient was given histidine treatment. During the treatment the symptoms got definitely worse and the patient had hematemesis twice which she never had before. So after the sixteenth injection operation was inevitable and a prepyloric resection with antecolic anastomosis was done on 3-2-37 by Major Ebden, for an indurated pyloric ulcer.

Case No. 16.—Bh. B., a male student 18 years old was admitted on 16-3-37 for the treatment of severe dyspepsia and painful sensation in the epigastrium of eight months' duration. Patient gave a history of occasional vomiting with relief and marked loss of weight since the onset of the disease. X-ray showed an ill-formed duodenal cap. A niche was found in the lesser curvature in the first and second pictures without a corresponding notch. Gastric analysis showed a moderate increase in the acid content. Occult blood was present in the stool. Histidine treatment was commenced, but as the patient got worse in the first week, it had to be supplemented with alkalies, condition getting worse, full treatment was refused.

REVIEW

The series is graphically represented in the Table.

The whole series may be seen from the table to consist of eleven duodenal ulcer cases, three gastric

	Before Treatment								After Treatment				
No.	1	2	3	4	5	6	7	8	9	10	11	12	13
	Gastric Symptoms	Barium meal and x-ray	Test meal	Occult Blood	Operation findings	Diagnosis	Total number of injections	Hospitalised or not	Gastric Symptoms	Barium meal and x-ray	Test meal	Occult Blood	Classification for cure
1	++	±	+	+	N.D.	D.U.	25	N.H.	−	±	−	−	++
2	++	+	±	−	N.D.	D.U.	25	N.H.	+	−	±	−	±
3	++	−	−	+	+	D.U.	22	H.	−	−	−	+	+
4	++	∓	∓	+	−	D.U.	25	H/N.H.	+	∓	∓	−	±
5	+	−	∓	+	+	G.U.	18	H.	−	N.D.	N.D.	−	++
6	++	+	∓	+	N.D.	G.U.	35	H.	++	N.D.	N.D.	+	−
7	++	−	−	+	N.D.	D.U.	25	N.H.	+	+	−	+	±
8	++	−	+	+	+	J.U.	21	H.	−	N.D.	−	−	++
9	++	−	∓	∓	N.D.	D.U.	25	N.H.	+	−	−	+	±
10	++	+	∓	−	N.D.	D.U.	25	N.H.	−	+	+	+	±
11	++	−	−	+	+	J.U.	25	H.	+	N.D.	N.D.	+	±
12	++	−	+	+	N.D.	D.U.	25	H.	+	N.D.	+	+	±
13	++	+	−	+	N.D.	D.U.	25	H.	+	N.D.	±	+	±
14	++	+	+	−	N.D.	D.U.	25	H.	−	N.D.	+	+	±
15	++	+	−	+	+	G.U.	16	H.	+++	N.D.	N.D.	N.D.	−
16	+	+	∓	+	N.D.	D.U.(?)	25(?)	H.	+++	N.D.	N.D.	−	±

ABBREVIATIONS

Columns 2, 3, 5, 10 and 11.

N.D. = Not done.
± = Definite evidence of ulcer.
− = No evidence of ulcer.
± = Nil abnormal.
∓ = Suggestive of ulcer.

Column 5.

− = Operation showing presence (+) or absence of ulcer.

Column 6.

G.U. = Gastric ulcer.
D.U. = Duodenal ulcer.
J.U. = Jejunal ulcer.

Column 13.

++ = Completely cured.
+ = Relieved of symptoms.
± = Status quo.
− = Harmful.
H. = Hospitalised.
N.H. = Not hospitalised.

and two jejunal. Each of these was given a full course of 21 to 25 consecutive daily injections except in the cases of 5, 15 and 16. Judging the symptomatic, radiological and biochemical evidences, only three cases (1, 5 and 8) can be classified as 'cured.' In one case (3) there was only symptomatic relief. In the majority of cases, *i.e.*, in ten, the condition of the patient showed neither improvement nor otherwise. Two cases (6 and 15) got definitely worse after the treatment. At the end of histidine treatment, it is claimed that the patients rapidly put on weight, but in the present series, however, cases 1 and 9 only put on weight. In the majority of cases, the symptomatic relief was found after the first few injections, but they were followed, sooner or later, by the recurrence of symptoms.

The effect of histidine on gastric acidity in this small series is very varying. But two cases deserve mention (7 and 13) in that the acidity after treatment was far higher than before the treatment. These findings are more in consonance with those of Martin (1936) and Sandweiss (1936), than those of Stolz

and Weiss (1935), Gardiner (1936) and Rafsky (1935).

Only one of the cases (8) showed a marked reaction after the commencement of the treatment. Such reactions are not usually reported except occasionally, Sandweiss (1936).

DISCUSSION

Aron's observations were not unanimously confirmed. Aron's experiments have also been repeated by Barrey and Florey (1936), the experimental animals being cats and pigs, but the results were different from those of Aron.

In the deductions of Aron's animal experiments, one may find some lacunæ, for, the number of animals on whom the injections have been reported to be tried was very small. Moreover, the assumption that all the animals, on whom the operation of duodenal drainage was done, should necessarily have had peptic ulcer is open to question.

The soundness of the arguments in the hypothesis formulated by Aron, has also been adversely criticised. In the operation of duodenal drainage, on which the histidine deficiency theory of ulcer is based, there is not only disturbed protein metabolism, but also disturbed carbohydrate and fat metabolism due to the absence of pancreatic amylase and lipase as well as the duodenal secretion in the jejunum. Moreover, the jejunal ulcers may be accounted for, partly at least by the mechanical factor (Mann and Williamson (1923), and susceptibility of the jejunal mucosa for ulcer formation; as it was found that the farther from the pylorus, the more is the mucous membrane of the small intestine susceptible to ulcer formation by the gastric juice (Mathews and Dragstedt, 1932).

Moreover, according to Aron's hypothesis, any method by which the trypsinogen is not made to act on the food at the jejunum should produce peptic ulcers at the jejunum. But modifications of the operation of duodenal drainage fail to show the same results. When the common bile duct and the pancreatic duct are transplanted into the terminal ileum leaving the duodenum *in situ*—only 50% of the animals developed peptic ulcer (Mann and Williamson). Moreover evulsion of the pancreatic ducts, preventing the pancreatic secretion from reaching the intestinal tract, is rarely followed by ulcer formation (Holmer, 1935).

Though it is claimed that the therapeutic effect of histidine may be used as a differential diagnostic test of simple peptic ulcer from a malignant one and that 'no rigid diet and no interference with normal everyday routine of the patient need be enforced', in histidine therapy, clinically, the consensus of opinion seems to be that probably histidine therapy can at best be an extra-artillery' to the time honoured alkali regimen. Feldheim (1936), Sandweiss (1936), Eads (1936), Dovson (1936), Lombardi (1936), Frydman and Iwanter (1936) and Pieree Hinemand (1936). But some others like Jacques Spira (1936), Izod Bennett (1936) and Kirbey Martin (1936), opine that histidine does not find a place in gastric ulcer therapy as such. The omcial Council of Pharmacy and Chemistry of the American Medical Association have not accepted Larostidin, a brand of histidine, as one of the new and non-official remedies. From the present series also, one is justified in drawing a conclusion that histidine may not find a place as a 'cure'. Even the established ulcer cures like the Sippey regimen do not stand the criticism on the authenticity of calling it a 'cure'—for Emery and Monroe (1935), on the basis of the experience of 1,435 cases of peptic ulcer find that the results were satisfactory in 90% of the cases and conclude that 'none of the present methods of treatment do more than assist in the induction of remission, no matter how strict the medical schedule or how radical the operation.' Many an ulcer cure have been introduced and none stood the test of time. Vaccineurin, novoprotein, aolan, various strains of organisms and vaccines, pepsin, sodium benzoate, emetine hydrochloride, hæmoprotein, sodium citrate, parathyroid extract, insulin, metaphen, aluminium hydroxide, mucin, powdered okra and silicon dioxide were some of the legion. Probably histidine also, in course of time, will be relegated to the above list.

SUMMARY

Sixteen cases of peptic ulcer have been treated with histidine. The results have not been very successful.

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THE INCOME TAX AMENDMENT BILL

The Income Tax Amendment Bill is now being circulated for opinion. At the next session of the Indian Legislative Assembly, this bill will probably be referred to a Select Committee, and its fate will be decided at a special session of the House in November next.

The amendments proposed are primarily based on the Income Tax Enquiry Report of 1936, and are modelled mainly on the Income Tax laws prevailing in the United Kingdom. Wherever there has been a departure, it has been mostly against the interest of this country or the assessee.

When a memorandum was submitted in 1936 before the Expert Committe, the representatives of the I. M. A. did not take up the question of general policy, but dealt only with matters referring to practices.

After the report was issued, the Association submitted to the Central Board of Revenue amongst other things its objections to: (1) joint assessment of the incomes of husband and wife, (2) the minimum taxable income and (3) lack of relief on abatement as prevalent in the United Kingdom.

Now that the bill is before the country, we feel that we should take up these points once again, leaving other objectionable features of the bill to specialists more competent to deal with them.

I. Minimum Taxable Amount and Abatements:

Though the figures of minimum taxable income do not come within the purview of this bill (it being considered under the Finance Bill each year), the figures recommended in the Enquiry Report as "slab scale" will probably be in force.

The question of reliefs or abatements as they are called, is a very important one. We are not experts in the theory and practice of Income Tax, but we gather, the idea of taxing income is for revenue of State, not to kill the goose that lays the eggs but to encourage the earning of income by giving some concessions also; to adjust the taxation so that low incomes are spared ensuring a higher and healthier general standard of living, and taxing the rich who live in luxury and superabundant comfort, at a much higher rate.

The abatements allowed in the United Kingdom are as follows:—

"Every individual is entitled to claim certain allowances irrespective of the amount of his total income. For this purpose the total income from all sources should be set out and the following deductions made therefrom:—

(1) Earned income allowance of one-fifth of the amount of earned income; maximum £300.

(2) Personal allowance of £100 if unmarried or £160 if married.

(3) Children allowance of £60 for each child under 16 years of age or still receiving full-time education. No allowance where income of child in own right exceeds £50 a year.

(4) Allowance of £50 to an unmarried person who has living with him his widowed mother or other female relative taking charge of a younger

brother or sister in respect of whom an allowance can be claimed under (3) above.

(5) Allowance of £50 to widower (or widow) who has living with him a female relative acting as housekeeper, or some other female person if no relative available.

(6) Allowances of £25 for maintaining (a) a dependent relative incapacitated by old age or infirmity or (b) his or his wife's widowed mother or (c) his daughter upon whose services he is compelled to depend, provided that the said relative's own income does not exceed £50 per annum.

"After these deductions from the total income, the first £135 of the balance is taxable at 1/7 in the £ and the remainder at 4/9 in the £, a set-off being made in respect of any tax deducted from dividends, etc.

"It should be noted that if the declarant (or his wife) is of 65 or more, and the total income does not exceed £500, an additional allowance can now be claimed by applying the "earned" income rebate to all income whether earned or not."

From the above figures, simple calculation will show that in United Kingdom, a single person earning Rs. 2,150 (about £165) without any dependents, pays about Rs. 32/- as Income Tax, about the same as is proposed here.

But if he has any dependent, say old mother, or a brother or a sister he pays nothing at all. If a person is married, say with 3 children and one or two dependents, up to an earned income of about £550 (*i.e.* Rs. 7,150) he pays no Income Tax in United Kingdom, whereas, in India, he will have to pay about Rs. 350.

Thus the myth, that taxation is very low in India, is exploded, at least so far as low incomes are concerned. It will be evident that though the Expert Committee in a few sentences (para b, page 15 of their report) have brushed aside the case for allowances for wife and children, etc., the net result will be a low standard for such families—resulting in the continuance of a C_3 nation. In view of prevailing malnutrition, increasing incidence of tuberculosis and other diseases, this is a particularly unwise step. For the sake of the health of the nation, a different policy should be pursued, and abatements or allowances for wife, children, etc., should be introduced.

II. Joint Income of Husband and Wife:

Regarding this question the bill appears to be unfair, in respect of the *earned* income of the wife. The allowance of Rs. 500/- a year, *i.e.*, about Rs. 40/- a month, may sound very liberal on the basis of Rs. 1,800/- a year (as discussed by the experts in their report). As, however, this sum seems to be the maximum allowable, irrespective of the amount of income, there does not appear to be any fairness about the proposal. This allowance should be proportionate to the income, say 1/3, 1/4 or even 1/5th. Only then will it be logical, there will be some inducement on the part of the wife to earn, and the measure will not kill the goose that will lay the golden egg for the State.

The assessment on the basis of joint income should, however, cease in the event of husband and wife not living together.

III. With reference to particular problems of the profession regarding methods of book-keeping outgoings, etc., provision already exists in the Act, and improvements have been suggested in the amendment. What is needed, is classification of these points—specially with regard to discretionary powers of Income Tax Officers. If it is not possible to do so in a bill, the object may be even better served, by the Central Board of Revenue issuing detailed instructions to officers of the department.

On the whole, the amendments proposed, in many respects, are distinct improvements on the old Act, and it is hoped that if the suggestions of the Indian Medical Association are accepted, along with others that may be offered by other competent bodies, the new Act will bring relief to quarters where it is urgently and badly needed. It may once again be pointed out that a few rupees a month in case of families with a low income, may mean much more than is usually supposed. Even a few pints of skimmed milk may make all the difference between health and disease amongst the children.

CURRENT MEDICAL LITERATURE

MEDICINE

Influence of Digitalis in Angina

Gold and others (*Journal of American Medical Association*, March 19, 1938, page 859) report on the investigation of the effect of digitalis on 120 patients with effort angina and no congestion. Digitalis was given in adequate doses, upto 9 grains of dried leaf daily and was alternated with the use of placebos. Full precaution was taken to prevent the patient from knowing what he was taking and if a single course of digitalis caused improvement a second or repeated courses were given later, the color and taste of the preparations being changed. In 30% of the cases the pain seems to be lessened in severity and frequency by the use of digitalis; in 15% it was increased. These alternations were not uniform in the same patients when the test was repeated and similar results were obtained by the placebo. Thus it appears that digitalis is without effect, either good or bad on angina of effort.

Electrocardiographic Changes In Dogs Following The Administration Of Magnesium Sulphate

Miller and Dallen (*Journal of Laboratory and Clinical Medicine*, June, 1938, page 914) from experimental studies in dogs observe that the intravenous injection of magnesium is characterized by an early acceleration of the heart-rate followed by definite slowing with delay in auriculo-ventricular and ventricular conduction time and increased excursion of all the complexes and that these effects are temporary and do not last longer than an hour. Respiration ceases before cardiac activity stops.

Tuberculous Tracheobronchitis

Warren and others (*American Review of Tuberculosis*, March, 1938, page 315) from the study of results of bronchoscopic examination performed on 198 tuberculous patients point out that there were in 71 instances ulcerative or stenotic lesions of the bronchus or trachea, that of 57 cases of tuberculous bronchitis or tracheitis treated 34 healed, 10 progressed, 4 did not improve and 9 are still under treatment. They further observe that in 31 patients the sputum was positive though there was apparent control of the parenchymal disease and in this group the healing of the ulceration was soon followed by negative sputum in 22 out of 26 healed cases. The authors hold the view that every favourable result can be obtained in tuberculous tracheobronchitis by electrosurgical and chemical cutery.

The Use Of Mercurial Suppository As A Diuretic

Flexner (*Annals of Internal Medicine*, May, 1938, page 1962) reports on the diuretic effect of mercurin suppositories used on 20 occasions in 10 cases of varying degree of cardiac decompensation. These patients had routine treatment of rest, sedatives, restriction of fluids and digitalis. In 85% (17 instances) a diuresis ranging from 1,950 c.c. to 8,750 in 24 hours resulted from the use of the suppositories. Of the three failures two had renal complications and one had delayed diuresis following the use of suppository (third day). In two cases of hepatic cirrhosis the diuretic effect was not consistent and moreover there was rectal discomfort after its use. The author points out that the mercurin suppository is an effective diuretic agent in selected cases; that it is most efficacious when combined with ammonium chloride and it should be very cautiously used in cases with renal damage.

Emergencies In Cardiac Disease

Gosse (*Practitioner*, April, 1938, page 337) writes that cardiac emergencies are usually confined to pain in the chest, to shortness of breath and to a consciousness of irregularities of cardiac rhythm. In *coronary thrombosis* pain is most agonizing and continuous—there is no pain in any disease more difficult to abolish than that of cardiac infarction. Electrocardiogram is of great value in diagnosis. Treatment consists of absolute rest for at least 6 weeks and relief of pain by full doses of morphine which is to

be repeated as often as necessary. Nitrites do not relieve pain but may be of value when paroxysmal dyspnœa is disquieting and digitalis also is of no use unless complicated by auricular fibrillation or flutter. *In angina of effort* nitrites are useful and are better combined with capsicum for the relief of flatulence which so commonly accompanies angina. *Dyspnœa of cardiac origin* should be diagnosed early and here an x-ray of the chest is of primary importance. Treatment of dyspnœa consists of restricted exertion with digitalis. Potassium iodide will help some patients. The combination of theobromine sodium salicylate with phenobarbitone is perhaps the most useful of the new remedies: Euphyllin is also worthy of trial. *Cardiac asthma* is a paroxysmal dyspnœa in a patient with gross heart disease who has not suffered from previous bronchial asthma and this is the result of left ventricular failure. Atropine gr. 1/100, repeated, is probably the best treatment; morphine may be necessary but adrenalin should be avoided. Venesection followed by 50 c.c. of 50% glucose given intravenously may tide over a crisis. *Auricular fibrillation* and *dropped beats* are the two common changes in the rhythm causing an emergency. It must be decided if the auricular fibrillation is paroxysml or established. If the former prophylactic quinidine sulphate 3 grains once or twice a day may be a satisfactory prophylactic for many months. If established digitalis in adequate doses is almost specific. It is undesirable to attempt to restore a normal rhythm in established fibrillation by quinidine when (1) there has been any evidence of emboli, (2) there is severe valvular disease, (3) the heart by an x-ray is found to be grossly enlarged and there has been previous congestive heart failure. Dropped beats by themselves are harmless. When the heart is not enlarged or when the patient has a good response to effort he must be reassured and treatment will then consist of improvement of the general health and correction of any dyspeptic trouble. Stimulants or sedatives are to be chosen according to the needs of the patients.

On The Treatment Of Cholecystopathy

Boas (*Wiener Medizinische Wochenschrift*, Nos. 1/2, 1938) writes that in acute biliary colic there is an attempt to eliminate biliary concretions, *i.e.*, congested and infected bile and our aim should be to help nature in the elimination. Opium is to be avoided as it reinforces the tonus, *i.e.*, spasm. Chloral hydrate 0·5 gm. with 0·25 mgm. of atropine sulphate in tea or possibly by the rectum every 2-3 hours will be of much benefit. Soporifics such as Medinal, Somnifen, Evipan, etc., are also useful. Local application of heat has a spasmolytic effect but is ineffective when there is a fever, pain due to presure, jaundice, a high degree of urobilinogenuria or porphyrinuria and should be replaced by application of cold. In definite inflammatory disease of the liver and gall-bladder application of ice-bag day and night is preferable. Three to four tablespoonful of paraffin oil with a few drops of oil peppermint for several days until the trouble is over cause profuse non-irritating motions and have a depleting (cholagogic and choleretic) effect on the inspissated bile. This is known as "Paraffin thrust". In cases with jaundice insulin with grape sugar should be used at the same time. Chronic biliary and liver diseases:—overloading of the stomach, iced foods, very acid or abnormally spiced foods, food which is no longer fresh or has been badly cooked or an unsuitably mixed diet may provoke acute attacks. Diets should be essentially rich in carbohydrates. The general prohibition of eggs and every kind of fat is only justified with obese patients. Olive oils and yolk of eggs are excellent cholagogues. Moderate quantity of fresh fruits are permissible. In hypoacidity hydrochloric acid, lemon juice, meat extract are helpful. An ample supply of fluid for irrigation of bile passages is desirable. Fruit is very beneficial whereas anything which disturbs intestinal peristalsis (cereals, pastry, banana) should be avoided. Permanent results cannot be achieved, however, without suitable laxatives which have in addition a cholagogic effect. The best results are obtained with "Paraffin" thrust" for 2 to 3 months. The numerous cholagogues, choleretics and disinfectants on the market are far inferior to the said simple remedies. (*Ars Medici*, April, 1938).

SURGERY

The Diagnosis Of Tumours Of The Central Nervous System

Holmes (*Practitioner*, June, 1938, page 742) deals with the subject under the two main heads, *viz.*, intracranial tumors and spinal tumors. An intracranial tumor may usually manifest its presence in

three ways: it may produce the signs of a slowly progressive local lesion (as a slowly progressive hemiparesis) or it may give rise to increased intracranial pressure and the symptoms thereof or finally to periodical fits resembling ordinary epilepsy. It must be recognised that cerebral tumor is by no means synonymous with increased intracranial pressure. Headache, vomiting, papillœdema, slow pulse rate and progressive blunting of the mental capacity passing on to stupor and coma are present only in 60% of the cases of cerebral tumor and only too often cases are left untreated until the appearance of such grave symptoms as blindness or paralysis because at the beginning there was no evidence of increased intracranial pressure. Those symptoms along with hallucinations, vertigo, hemianopia, tinnitus and deafness may sometimes be of some localising value. To diagnose a case of intracranial tumour one is to assess the value of these symptoms and to examine the patient thoroughly and employ the following laboratory tests, *viz.*, plotting of the visual field, blood count, examination of the cerebrospinal fluid for manometric reading of the pressure, cell count, protein and gold tests and W. R. and radiological investigations. The cerebrospinal fluid examination is of primary importance and the reading of the manometric pressure should be done under novocaine anæsthesia with the patient lying on his side and his body quite relaxed. Radiography of the skull will consist of stereoscopic lateral, antero-posterior and postero-anterior views. Ventriculography (skiagrams after replacement of cerebrospinal fluid in the ventricles by air), encephalography (air introduced through lumbar puncture) and arterial encephalography (demonstration of cerebral arteries radiographically by introducing 20% thorium dioxide into the carotid artery) are some of the newly employed diagnostic methods (though not altogether easy and harmless ones).

Spinal tumors produce symptoms of compressions and these arise in the following order:—weakness and spasticity, then impairment of sensation, position sense and passive movements, temperature sense, pain and touch are affected in progression. Defective sphincter control often precedes and sometimes follows sensory loss which generally has a sharp upper level depending on the site of the tumor. Radiography of the vertebral column may be of great value. Sometime the exact level of the tumor may be shown radiologically by injecting lipiodol (not more than ½) c.cm. because it is very painful) into the cisterna magna and allowing it to flow down to the level of the block and this method is particularly useful in cases with indefinite sensory level.

Lung Abscess: Causes of Death

Rines and others (*Annals of Surgery*, June, 1938, page 753) from an analysis of the causes of death in one hundred consecutive fatal cases of lung abscess note that the factors responsible are, in the reverse order of their importance, anæmia, empyema and spreading pneumonitis and that these factors can be controlled. Anæmia is controlled by transfusion; empyema is controlled by instituting surgical treatment early in superficial lesions and entirely avoiding the needling of the chest; spreading pneumonitis may be controlled by avoiding attempts at drainage during the acute stage, by avoiding compression therapy especially when the cavity is incompletely drained, by avoiding measures such as intermittent postural drainage and by avoiding surgical drainage in acute stage and at any time at all in deep-seated abscesses. The results obtained are best when a well-planned treatment consisting of supportive measures, bronchial drainage and surgical drainage according to the proper indications and suited to individual cases is restored to.

Empyema In Children

Willis (*Annals of Surgery*, May, 1938, page 739) summarises in the following lines his observations on the results of treatment in empyema in children: "(1) Empyema cases should be diagnosed and treated early by aspiration and thoracotomy punch for early cure. (2) The most valuable four clinical signs are dullness, absent or diminished fremitus, diminished expansion and displacement of the apex of the heart. (3) The free use of roentgenograms and flouroscopic visualisation are indispensable aids in diagnosis and treatment. (4) Rib-resection in the children should be abandoned except in rare cases and then only after aspiration or thoracotomy have been thoroughly tried. (5) Intrathoracic tension should be gradually reduced. (6) The thoracotomy tube should not be removed until the cavity is obliterated. (7) The patients treated by thoracotomy require close attention of skilled and

interested attendants. (8) Blood transfusions are life-saving in debilitated children."

Sulphonamide Chemotherapy In Genito-Urinary (Non-Gonococcal) Infections

Cokkings (*British Medical Journal*, May 28, 1938, page 1151) reports on the successful results obtained by sulphonamide containing chemotherapeutic substances, specially one called Uleron which is a di-sulphonamide, in 57 cases of genitourinary infection (non-gonococcal). In a group of 26 cases of urethritis and four of epididymitis (both non-gonococcal) there were one and three failures; in another group of twelve cases of 'primary' urinary infection consisting of a mixture of acute and subacute pyelitis and cystitis there were one and three relapses; in the third group of fifteen cases of secondary urinary infection of which nine were cases of senile prostatic enlargement, four with urethral stricture, one with epididymitis and one with vesico-colic fistula two-thirds of the prostatic cases were benefited in both pre- and post-operative urinary sepsis though relapses were common. Two prostatic and two stricture cases completely failed to respond.

OBSTETRICS AND GYNÆCOLOGY

The Treatment Of Placenta Prævia

Lloyd and Gissen (*British Medical Journal*, June, 11, 1937, page 1258) mention the standard method of treatment of placenta prævia followed at the Queen Charlotte's Maternity Hospital and review the results obtained in a group of 143 cases (Group A) under the standard scheme and compare them with those of another group of 143 cases (Group B) treated immediately preceding the start of the scheme. The mortality rate in Group A cases was 1·4% as opposed to 5·6 in Group B cases and this striking decrease in the mortality rate is due to (1) co-operation and team work made possible by standardization of treatment, (2) prompt arrest of severe hæmorrhage by plugging the vagina, (3) replacement of blood loss by transfusion and (4) treatment of shock before delivery. The standard method of treatment adopted consists of (1) exclusion of toxæmia; (2) blood grouping of all cases with a pulse rate of 100 p.m. or more prior to vaginal examination and preparation made for transfusion; (3) vaginal examination under light anæsthesia:—if there is central placenta prævia cæsarian section is to be done: bleeding is controlled by packing cervical canal and vagina with gauze with counter pressure effected by a tight abdominal binder or T-shaped perineo-abdominal bandage, general condition is to be improved by transfusion and morphine: if there is a marginal or lateral placenta prævia the membrane should be ruptured artificially whether the patient is in labour or not and the vagina should be plugged if there is profuse and continuous bleeding; (4) replacement of the blood loss by early and adequate transfusion. The authors note that the packing of the vagina should be efficient with gauze in form of rolls 4 inches wide and 6 yards long, soaked in 5% solution of dettol. The vagina should be packed tightly (usually 3 rolls are necessary for primigravidæ and 5 for multigravidæ) and the packing should be left for 24 hours or until it is expelled during labour by the presenting part. Catheterisation of the bladder is necessary when the packing is in position and repacking is necessary only in a few cases.

Ætiology Of Thrombosis And Embolism

Dougal (*Journal of Obstetrics and Gynæcology of the British Empire*, June, 1938, page 425) in discussing the various factors responsible for thrombosis and embolism in special relation to the puerperal and post-operative conditions observes that the tissue trauma and sepsis are the two primary factors, that slowing of the circulation is a very important predisposing cause of thrombosis, that certain changes occurring in the blood during puerperium and other factors, *viz.*, age, sex, weight, seasonal factors, etc., though contribute to the formation of such lesions, the latter will not occur unless one of the more important factors, *viz.*, tissue-trauma or sepsis be present.

Normal Expectancy In Extremely Obese Pregnant Women

Mathews and Brucke (*Journal of American Medical Association*, February 19, 1938, page 554) in reporting on the study of 200 hundred pregnant women all weighing more than 200 pounds in a series of 6,025 consecutive deliveries observe that plevic measurments were usually normal, albuminuria was present in 35%, hypertension in 35%, glycosuria in 4·5% œdema specially of the lower extremity in

43·5% with higher incidence of headache, dizziness and gastro-intestinal disturbances. Abnormal presentation (mainly occipito-posterior and breech) was present in more than 26%, the labour was usually prolonged (because of malpresentation and primary uterine inertia), the incidence of operative delivery was more than four times that of total cases treated during the period under review. The maternal morbidity was 20%, the maternal mortality 1%, and the fœtal mortality 12·3%. Thus pregnancy in extremely obese cases presents definite risks.

Post-Partum Necrosis of the Anterior Pituitary (Pathological and Clinical Aspects)

Sheehan and Murdoch (*Journal of Obstertrics and Gynæcology of the British Empire*, June, 1938, page 425) from personal experience and the review of the literature write that extensive ischæmic necrosis of the anterior pituitary is not an uncommon post-mortem finding in women who die in puerperium of collapse due to severe hæmorrhage and signs of healed necrosis in the anterior pituitary are also found in cases who die of Simmond's disease which originated long time ago from delivery which on enquiry was found to be accompanied by severe bleeding and collapse. Clinical investigations along with two lines, *viz.*, (1) to look for evidence of hypopituitarism in patients who have survived hæmorrhage and / or collapse at delivery and (2) to find whether there is a history of hæmorrhage and / or collapse at delivery in patients who have evidence of hypopituitarism coroborate the pathological findings mentioned above. A follow-up of 128 patients who had varying degrees of collapse at delivery showed in 41 cases symptoms of pituitary insufficiency (these symptoms are due to healed necrosis and are proportional to severity of the extent of necrosis). A reverse follow-up of 15 women who had symptoms of hypopituitarism showed that in 13 of them the condition dated from a delivery in which there was severe hæmorrhage.

Induction of Labour by Puncture of the Membranes (Review of 357 Cases)

Tennent (*Journal of Obstetrics and Gynæcology of the British Empire*, June, 1938, page 509) analyses the results of the surgical induction of labour obtained by the puncture of the membranes in Professor Hendry's Unit of the Glasgow Royal Maternity and Women's Hospital during the last six years ending in December, 1936 and observes that puncture of the membranes is fairly reliable and efficient (about 70%) method of inducing the labour, that labour is not usually prolonged or difficult after puncture, that the risk of sepsis is always present as in 5 of the septic cases puncture of the membranes was the only interference and that there is possibility of prolapse of the cord specially in cases of abnormal presentations or when the vertex is not fixed.

VENEREAL DISEASES AND DERMATOLOGY

Detection of Syphilis in a Urological Clinic

Friedam and Mazer (*American Journal of Syphilis*, May, 1938, page 340) report on the investigations on 252 unselected patients in the urological out-patient department of the hospital of the University of Pennsylvania. By the routine employment of the three following methods, viz., detailed and persistent questioning for a history of syphilitic infection or treatment, careful physical examinations including dark-field study and routine blood serologic tests, syphilis was detected in 29% of the cases. They further noted that 40% of the syphilis found was hitherto entirely unknown and varying but significant percentages of syphilis were found in all groups, in stages of gonorrhœal and other urological conditions.

Gonococcic Endocarditis

Wiliams (*Archives of Internal Medicine*, 1938, page 26) writes from his experience in the Vanderbilt University Hospital that the gonococcal endocarditis is not so rare as is supposed to be as it was present in 26% of the patients with bacterial endocarditis and in 0·1% of all patients coming to autopsy. Ten of the twelve cases reported came to necropsy. There was no pericarditis: areas of focal necrosis in myocardium, sometimes amounting to true miliary abscess formation, were present in 6, extravasation of blood into the myocardium in 1: the valvular involvement consisted of erosion, ulceration of the leaflets with or without rupture of the cusps (2 cases); five had mitral lesion, four had aortic and one combined lesion: spleen was usually large and the liver in 7 cases weighed over 1,700 gms. glomerular nephritis was present in 8 patients and renal infarcts in 2. The differential diagnosis is difficult

and the prognosis is grave. The onset of endocarditis in relationship to the primary infection was variable. The clinical picture was that of sepsis with endocarditis with a rapidly progressing course.

Uleron in Gonorrhœa

Grutz (*Munchener Medizinische Wochenschrift*, No. 31, page 1201) found that with no treatment other than oral administration of Uleron the gonococci disappeared in most cases in 1-3 days, occasionally after 4-5 days. On the first day 0·5 gm. three times a day was given. From the second day onwards 0·5 gm. four times a day and, if necessary, even larger doses were given. Posterior urethritis and prostatitis disappear also. In a few days the second sample of urine clears completely and leucocytes disappear. Double epididymitis and gonococcal arthritis clear up in a week merely by the treatment with the tablets. Of the thirty-six cases of gonorrhœa treated chemotherapeutically pure and simple, twenty-four were cured, in three cases the results were uncertain and the treatment completely failed in nine cases. Crutz, therefore, counts two-thirds success and one-third failures. Rash occurs occasionally.

Treatment of Gonococcic Vaginitis With Estrogenic Hormone

Iinde (*Journal of American Medical Association*, March, 1938, page 1034) in reporting on the results obtained by amniotin in 175 patients with gonococcal vaginitis observes that all except 16 were cured by such treatment. The vulva is washed at the daily bath but no vaginal irrigations or instillations are used. Suppository containing 1000 international units of amniotin is used, one suppository being introduced into the vagina daily at bed-time and this is continued over about a month. A follow-up of 100 cases from 3 months to 2 years and a half showed 98 of them doing well and there were found no ill-effects due to the treatment done. The authors maintain that the factors responsible for the beneficial effect of the estrogenic hormone in gonococcic vaginitis are increased acidity of the vagina and covering of the same with thick epithelium preventing re-infection of the subepithelial tissues and permitting inflammatory process in them to subside.

PEDIATRICS

Prophylaxis Against Measles With The Globulin Fraction Of Immune Human Adult Serum

Karelitz (*American Journal of Diseases of Childhood*, April, 1938, page 768) writes that globulin fraction of immune human adult blood serum is effective in prophylaxis against measles. The globulins were removed from three pools of measles immune adult serum and were prepared in volumes equal to one-sixth and one-tenth of the original volume of the serum. Ninety-eight children susceptible to measles intimately exposed to the disease were tested with the globulins thus obtained and the results were definite and striking. No local or general reactions were noted by the injection of the concentrated filtered preparations. The methods of preparations are given in detail. The author maintains that this treatment with globulin fraction of immune adult serum is recommended in the prophylaxis of measles for the following reasons: (1) it has been efficacious in doses easily calculated from the known indicated dose of immune adult serum and it is easily prepared from immune serum which is available in abundance at all times, (2) the amount of injection is small as compared with the amount of immune serum injected, (3) the danger of infecting a child with syphilis, tuberculosis is eliminated (the infection occasionally occurring with the use of whole blood), (4) the reactions are less severe and results more uniform than those observed in cases treated with commercial solutions of placental globulin and (5) the solutions of adult serum can be transported and stored at ice-bag temperature without loss of potency for at least one year.

Collapse Therapy in Tuberculosis of Children

Siegel and Singer (*American Journal of Diseases of Childhood*, May, 1938, 924) report on the results of collapse therapy in 105 children with open tuberculosis (all had positive sputum and 95% had cavities) observed during the years 1928-1936: forty children improved, thirty-three remained unimproved and thirty-two died. Sputum was turned negative by pneumothorax alone in twenty one out of twenty-eight cases (70%) within three months and in all cases within six months after the start of collapse

therapy. Of the patients with isolated infiltrative tuberculosis (unilateral) 60% improved; of those with infiltrative tuberculosis with contralateral spread 22% improved and of those with disseminated tuberculosis 29% improved. The improvement depended more with the degree of collapse but also on the nature and extent of the lesion. Moderate or large amounts of pleural effusion developed in the course of pneumothorax in twenty-six cases (26·6%). Of eighty-seven untreated children with open tuberculosis admitted to the hospital between 1929 and 1936 and observed to date, 95·4% died, 1·1% were unimproved and 3% were improved. They conclude by noting that the results of collapse therapy are (a) a considerable increase in the number of improved children and (b) a prolongation of the span of life.

Infantile Hydrocephalus

Putman (*American Journal of Diseases of Childhood*, May, 1938, page 990) in reporting on the treatment of infantile hydrocephalus by endoscopic coagulation of the choroid plexuses observes that out of forty-nine operations made on twenty-six patients there was operative mortality in 10 cases, that operation proved more successful in certain types of cases than in others, that of the five patients who were mentally healthy before operation four survived and progressed normally in their mental growth, that infants who are demonstrably feeble-minded should not be operated on. This report is highly encouraging and invites further trial of the surgical treatment of the condition in which conservative treatment has hopelessly failed.

Anaphylactic Gangrene

Kohn and others (*American Journal of Diseases of Childhood*, May, 1938, page 1018) report of a case, who was sensitive to horse serum that developed extensive gangrene after repeated injection of horse serum at the same site (the reaction may occur if successive injections are made at different sites). The authors hold that the combined interaction of fixed horse serum antigen and its antibodies and bacterial toxin at the site of injection is the cause of extensive hæmorrhage and subsequent gangrene. This reaction though rare should make us cautious in using repeated injections of horse serum particularly if the patient is sensitive to it.

Sulphanilamide in the Treatment of Gonorrhœal Vulvovaginitis

Hoffman and others (*Journal of American Medical Association*, May 7, 1938, page 1541) in reporting on the treatment of gonorrhœal vulvovaginitis with sulphanilamide in a series of twenty-five cases observe that seven were cured in 17·3 days and nine in 42·9 days and only two of the nine remaining were cured by additional use of the drug. They further point out that in treating such cases more than two standard courses of treatment are useless and that children bear sulphanilamide extremely well.

THE ORIGIN AND GROWTH OF THE MATERNITY & CHILD WELFARE MOVEMENT IN BOMBAY

SIR MANGALDAS V. MEHTA, KT., O.B.E., F.R.C.P.I., F.C.P.S., F.C.O.G.

Honorary Principal Medical Officer, Nowrosjee Wadia Maternity Hospital, Bombay

Attention to maternity was almost unknown in Bombay about 30 years ago, and the starting of a maternity home was then considered an adventurous feat. In the olden days the woman was confined in an ill-ventilated and dark room in the house, and provided with dirty and torn rags for linen, because of the superstitious religious belief that anything coming in contact with the delivering woman was impure and therefore must be burnt and destroyed. It is only since the last 20 years that in cities and large district towns in the urban areas we hear of midwifery specialists, general practitioners, midwives and maternity hospitals and homes, and simultaneously the growth of health visitors and social workers in the cause of infant welfare. The movement originated in the city of Bombay where the majority of the populace are people drawn from mofussil who form the floating population of the city. The handicaps they suffer from in the city are numerous, the want of proper accommodation in one room tenements, lack of attendance and help at the time of delivery, and lying-in period are great factors in inducing them to seek outside help, particularly in view of the fact that the Hindu joint family system in the Presidency is rapidly breaking up, chiefly amongst the middle classes. The maternity homes not only provide this much-needed relief but also give skilful aid, which comes as a revelation to the women who seek advice; they also provide complete physical and mental rest and nutritious food; there is less suffering, more maternal care, and fewer after-effects with the result that the child receives a good start in life. Side by side with this, District Maternity Service was also made available in Bombay by the Municipality and Infant Welfare Society, but it never caught the fancy of the poor; for, while the poor suffered from want of space as the greatest handicap, the middle classes went without help and assistance at the time of delivery and during the lying-in period.

The advantages of a maternity home are so numerous and oustanding that the District Maternity Service seems to have had no place in the city. The people likewise have now overcome the prejudice and are not averse to it in small towns and in some villages also. They carry with them the memories of the benefits they received in the city and form, as it were, the nucleus of a new village area maternity education. As has been mentioned above, the working class in Bombay form a floating population with permanent homes in the villages. They often give great help in inducing their neighbours to seek aid on the latest and most approved lines. The rise of maternity homes in the district towns and big villages is due to the above two causes.

The Bombay Nursing Council has given a tremendous impetus to maternity work by organising the midwifery profession and raising it from the depths of ignorance and prejudice in which it had lain for centuries in this Presidency. The work is hard and arduous and can only be achieved by sending out batch after batch of qualified midwives to the mofussil. The *dais* no longer find favour in the city of Bombay and partly in larger district towns; their great stronghold is in the villages where no help is available for the women in distress.

In foreign countries the midwives are a highly trained and intellectual class of women who have a recognised position in society and whose occupation is looked upon as respectable and important. There is thus a wide difference between the conditions obtaining in Western countries and in India.

Motlibai Hospital—In 1849, the Government of Bombay opened a maternity home of 20 beds in the J. J. Hospital compound in charge of the Professor of Obstetrics at the Grant Medical College. In the year 1888, Bai Motlibai (through her son Mr.

Nowroji Manekji Wadia) placed at the disposal of His Excellency the Governor the site known as the Parsonage of Mazgaon, the building thereon, and a further sum of rupees 1½ lakhs in cash, for the construction of a charitable hospital. On the 22nd January of the following year plans and estimates amounting to Rs. 1,37,657 were sanctioned. The hospital was built to accommodate 40 patients at a cost of Rs. 1,52,061 and opened in March 1892, the present Motlibai Hospital.

Since then up to 1927 minor additions and alterations were carried out in connexion with this hospital. In 1927 Government approved of an extension to Bai Motlibai Hospital by 50 beds at a cost of Rs. 1,80,000, but owing to financial stringency no action was taken by Government. Finally in 1937, re-organisation of the Hospital has been sanctioned at a cost of Rs. 1,46,000. For a long time this Hospital was taken advantage of by women of the lower class for complicated labour only.

Cama Hospital—As far back as 1880, in the whole of India there were a few medical women in the North-West, Bengal and Madras but in the Bombay Presidency there was not a single woman with a medical degree.

With the help of Mr. Sorabjee Shapurji Bengali, Mr. Cummor Suleman and other Indian gentlemen, Mr. Kitterdge, an American businessman in Bombay, was successful in collecting a sum of Rs. 40,238 which rendered it possible to carry out the scheme for establishing a maternity hospital. In the meantime, Mr. Pestonji Hormusji Cama of Poona came forward with the munificent offer of one lakh of rupees to be expended in building a hospital for women and children, provided that a site for building and the cost of maintenance were borne by Government and that the hospital was placed under the charge of women doctors. Eventually this offer was accepted. Later Mr. Cama increased his gift to Rs. 1,20,000 and then again to Rs. 1,64,300.

The present site of the Hospital on the Esplanade Maidan was chosen and on November 23rd, 1883, the foundation stone was laid by H. R. H. the Duke of Connaught.

It had been arranged to begin the work at once and rooms for a temporary dispensary were taken in Churchgate Street. Mr. Cummor Suleman gave his assistance in the search of suitable premises and ultimately offered a gift of Rs. 20,000 with which to build a permanent dispensary in memory of his brother Mr. Jaffar Suleman, if Government would provide the site. A site on the market Esplanade was selected and granted. Mr. Cummor then put up a temporary building nearby for use while the Jaffar Suleman Dispensary was being erected. The Municipal Corporation gave a grant of Rs. 500 per mensem to maintain the dispensary of the hospital as part of the Cama Hospital, the proposed dispensary of the hospital being converted into a small ward. During the building of the Cama Hospital, the hospital work was carried on in a small bungalow at Khetwadi.

In 1886, the Cama Hospital for women was built with 12 beds entirely run by women doctors. In 1890, 12 more beds were added to make 24, by constructing the Albless Hospital. In 1909, the total accommodation came to 45 beds. In 1923, a separate septic ward of 22 beds was added to this. Both the Government maternity hospitals were meant for the lower class women and situated in the south of the island of Bombay.

Parsi Lying-In Hospital—The first private and sectarian venture was undertaken in 1887 by the establishment of the Parsi Lying-in Hospital under the able management of Dr. Sir Temulji Nariman for Parsis only, with a total accommodation of 50 beds.

From 1890-1910, the spirit of private enterprise for sectarian hospitals did not develop, and during this period of 20 years there was hardly any progress noticeable in maternity work for lower or middle class women.

Ruxmani Hindu Lying-in Hospital—In 1910, Dr. Sir Mangaldas V. Mehta opened his Ruxmani Hindu Lying-in Hospital for the Hindu community with 20 beds for middle class Hindus in the heart of the Hindu population. Since then doctors specialised in obstetrics started private nursing maternity homes, and such homes increased in large numbers till in the year 1932 there were 26 such institutions with 278 beds. The majority of these institutions were located in the south of the island and catered, at a moderate charge, to the middle class and clerical workers.

Municipal Maternity Homes—About 1911, the Marchioness of Willingdon launched a scheme for maternity and infant welfare, particularly in the north of the island. Three such homes were opened

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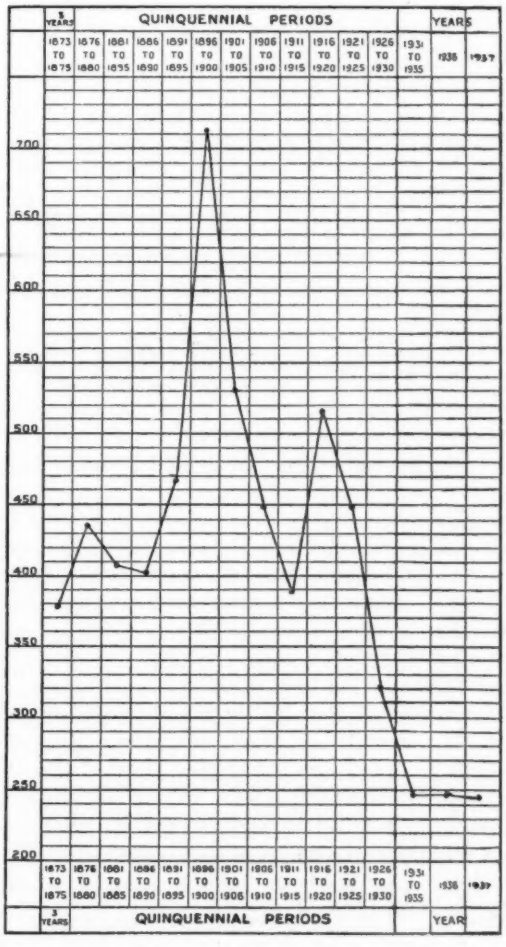
with 30 beds. These were afterwards called the Hajee Sabu Sidic's Maternity Homes at Bellassis Road, Imamwada, and Cadell Road, Worli. Since then the Bombay Municipality added two more maternity homes making up a total of five with an aggregate of 134 beds. These maternity homes are confined to normal labour only, and for operations and septic cases they co-operate with the three large maternity hospitals in the city of Bombay, *viz.*, The Nowrosjee Wadia Maternity Hospital, Motlibai and Cama Hospitals.

Nowrosjee Wadia Maternity Hospital—At the time of the Midwifery Commission of 1921, Dr. Sir Mangaldas V. Mehta pointed out that more than 75% of women of the mill-area migrated every year to their native place for confinement. This meant that Bombay city was being deprived of very great material for medical relief at the critical period of a woman's life, and this further meant a loss of material for the training of medical students and pupil midwives. Sir Mangaldas then approached Sir Ness Wadia, the mill magnate of Bombay, for financial help to start as an experiment a small maternity home of six beds in the heart of the mill area in Parel; as a result a whole building with four floors was hired to accommodate 35 beds. This was the result of the co-operation and sympathy enlisted by Sir Mangaldas of the important and influential persons interested in the welfare of workers in the various mills of Bombay. About the end of 1926, this Maternity Home was placed on a permanent footing by a special modern and well-equipped hospital of 150 beds, with the co-operation of Government, the Municipality and the Wadia brothers. The share of the Wadia brothers in the scheme for the building, equipment and land (19,500 sq. yards) came to six lakhs, and the Municipality and Government five lakhs each. The maintenance of the hospital is provided for by the Wadia brothers by an endowment of rupees 15 lakhs bearing an interest of Rs. 60,000 per year, and Rs. 35,000 each per annum by the Bombay Municipality and Government. The total contribution of the Wadia brothers has amounted to rupees 21 lakhs.

B. P. I. W. Society—The Bombay Presidency Infant Welfare Society founded in 1921, though primarily intended for the welfare of infants and children, found it necessary in 1929 to undertake the starting of maternity homes and also ante-natal clinics. The Bombay Presidency Infant Welfare Society started its first maternity home at Wadi-bunder in co-operation with the Bombay Port Trust in 1929, and by the end of 1932, they added two more maternity homes in B. D. D. Chawls at Worli and DeLislie Road in co-operation with Government. The total number of beds in the three homes maintained by the Infant Welfare Society is 80, and they also are confined to normal labours, in the north of the island mainly for the industrial area of Bombay which was badly neglected till then. The Society at



Deaths in infants per 1000 births in Bombay 1873 to 1937.

present is maintaining in the city of Bombay three complete units consisting of (1) antenatal clinic; (2) maternity home; (3) post-natal clinic; (4) infant clinic; (5) milk depot and (6) anti-venereal clinic, 4 infant welfare centres, one creche and one health visitors institute for the training of health visitors.

The Society after it had gained experience in work in the city encouraged the starting of mofussil centres for maternity and infant welfare work; eight such centres were opened from 1923-35.

Bombay Mofussil Maternity, Child Welfare and Health Council—The necessity of expanding such work in the mofussil was being keenly felt. As the Bombay Presidency Infant Welfare Society had not the funds and the staff necessary for undertaking this work, a new Bombay Mofussil Maternity, Child Welfare and Health Council was formed in 1936; 25 centres and homes have been encouraged by this Council with financial grants and expert advice, and the work is expanding rapidly. The mofussil public and the practitioners find it convenient and advantageous to concentrate on centralisation and hospitalisation of their work, which provide better control and organisation.

The position to-day is that in the city of Bombay there are 14 public and free institutions with 486 beds, and 8 private semi-charity institutions with 155 beds, while the paying nursing homes are 61 in number with 667 beds. The total number of maternity institutions (both public and private charity with free beds) and nursing homes comes to 83 with 1308 beds. The total number of births registered during the year 1937 was 37·795; out of these 27·758 were delivered in maternity institutions in the city during 1937, *i.e.*, a percentage of 73·4 as against only 20 per cent. confined in maternity institutions in the year 1920. In the year 1920 the total number of births registered was 19·731; the maternal mortality was 427, *i.e.*, 0·4 per 1000 population, and infant mortality 10·896 or 552·22 per 1000 births. The maternal death-rate has been falling regularly and consistently and in the year 1937 the maternal death-rate was 0·1 per 1000 population, while the infant death-rate also has been steadily going down, *i.e.*, 244 per 1000 births.

According to the old time-worn customs and religious belief, *viz.*, that the delivering mother should not be touched, and therefore any one coming in contact with her would be polluted, the control of the delivery of women was entrusted to untrained and illiterate class of women, the *dai*, who in course of time monopolised the obstetric profession to the detriment of the mother and child. These *dais* successfully plied their trade by charm, astrological influences and exercised a strong control over the women folk. No medical practitioner, either allopathic, unani, or homœopathic could have access to the delivering woman in the presence of a *dai*.

Dais and their Training in Rural Areas

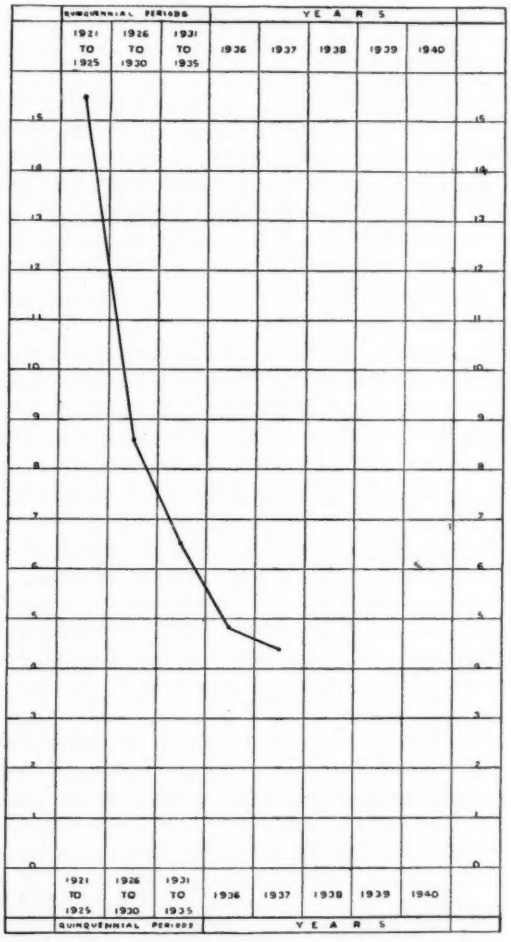
Attempts have been made to give elementary training to the *dais* by the Lady Wilson Village Dai Scheme under which they receive a few lectures on asepsis and are given demonstrations in delivery, if possible. *Dai* classes are being conducted in many district towns. The proportion of *dais* so trained is very small. The instructions given vary; but the minimum of education that is imparted seems to fall short of the actual needs of the day. Such of them as have taken longer than three months' course deserve more encouragment when they go back to the villages. As has been acknowledged everywhere the profession of the *dai* as such is a precarious one, and she has to supplement her living by manual labour. If she can be assured the minimum living wages by the Local or District Board or a philanthropic association and is properly guided and supervised from time to time, she can turn out very useful work and become capable of advancing the objects of the parent institution which gave her the training.

Many of the new centres are undertaking the training of *dais* with short and long courses. The most advanced in this respect is Satara District where about 1200 *dais* have received a short course and 60 have received a long course; efforts are being made by the District Medical Officer to organise them and unify their work. They also receive the much needed help and guidance from a committee and the medical officer.

Health Visitors

Infant welfare work is of much recent origin and has received an impetus by the entertainment of health visitors. The Health School of the Poona

Seva Sadan Society was first in the field and filled a much needed want in times of urgency. The training was in vernacular and the examinations were



Maternal deaths per 1000 births in Bombay 1921 to 1937.

locally conducted. The Bombay Presidency Infant Welfare Society started a Health Visitors' Institute in 1935, which is affiliated to the Bombay Nursing Council and the students receive a diploma after they pass examinations held by the Bombay Nursing Council. The course is of one year and the coaching is in English. All the passed students rapidly found service. This is the only Government recognised school in India.

Many more health visitors are needed in the districts—one with a little inferior training in vernacular and who does not aspire for higher pay is badly needed for district and rural work. The health visitor's work is very highly appreciated in the districts as they can approach the illiterate class more intimately than what any other person can do.

Infant welfare work and propaganda is on the increase in the Bombay City, but much more is needed. In the districts there is little infant welfare work done, and even the medical practitioners have a hazy notion of what it really means. They fail to realise that it is education of the mother from beginning to end, and therefore the centres often tend to degenerate into a place for doles and charity.

Societies for Helping Mothers

Societies to help the mothers do not exist. Social workers are badly needed as intermediaries between the health visitors and the family. The District Municipalities and Local Boards are very apathetic and what help they give is a mere pittance; and the propaganda of the health visitor is hardly ever followed up.

Education of the public and rousing the sense of health and of duty towards the children are badly needed. The funds available are meagre. Maternity work has caught the fancy of the public not solely because it lessens the mortality rate but because it means less expense and anxiety to the husband, who in most instances can ill afford the care and comfort necessary in connection with cases of confinement.

With my experience for the last 27 years in this line, I can say with confidence, that in about 5-10 years there will be a regular net-work of maternity homes and infant welfare centres in the mofussil, which will supply a long-felt need to the women of this Presidency, and thus lessen the maternal and infant mortality, provided, the various bodies working in this direction co-operate freely, and the sense of duty towards the mother and the infant is roused amongst the people, district municipalities, local boards and the Government of Bombay.

The old adage that "the child is the father of the man" should always be remembered and particular care should be taken to see that the mother who gives birth to a child is given all the care, treatment and convenience she needs, during the delivery period.

ASSOCIATION NOTES

Minutes or proceedings of Branches and Affiliated Societies intended for publication should be sent to the General Secretary of the I. M. A., Samavaya Mansions, Calcutta—EDITOR.

RAMNAD DISTRICT MEDICAL ASSOCIATION

REPORT FOR THE YEAR ENDING 31ST MARCH, 1938

OFFICE-BEARERS

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Vice-President—Dr. F. Ysander, M.D.
Secretary—K. S. Srinivasa, L.M. & S.
Joint Secretary—K. R. Ratnaswami, M.B. & B.S.
Treasurer—S. Subramanian, M.B. & B.S.
Members of the Executive Committee—Drs. E. Ivatts, T. S. Shetty, S. Rajaram Bharathi and N. Krishnaswami.
Auditors—Drs. R. Bheem Singh and M. S. Venkataseshan.

This Association was started in March, 1930, as the Chettynad Medical Association; the name was changed to the Ramnad District Medical Association in April, 1936. The Association was affiliated to the Indian Medical Association in December, 1935, and during the year under report the Association has been made a Branch of the Indian Medical Association from the 1st December, 1937.

Ever since the founding of this Association there has been a good co-operation among the service and non-service medical men in Ramnad District. The *esprit de corps* and comradeship among members have been marked after the advent of this Association, successive District Medical Officers of Ramnad taking interest in the growth of this Association. We have been fortunate especially this year to derive full benefit of the lead and guidance from our revered President Captain B. Dayananda Rao who has been taking a keen interest in the welfare of this Association. It is our earnest desire that more members should join and participate in all activities of the Association.

The year under report had 40 members who have paid their subscriptions in full—36 regular and 4 associate members; out of these 8 were from Government service, 11 from Local Board service, 4 from Rural medical practitioners, 2 from Municipal service and the remaining 11 were from the members of the Independent medical profession. The regular members have vote in business matters and are also members of the Indian Medical Association while the associate members are only members of the Ramnad District Medical Association without vote in business matters Every effort will be made to collect arrears of subscription due to the Association.

In spite of the fact that members practise at places several miles apart, the attendance at meetings (28·9) has been tolerably good though it could have been better. It is regrettable that some who could attend the meetings without much sacrifice of time or money have continued to be indifferent while members from far away places attended most of the meetings during the year; over 120 invitations have been regularly issued to all medical men in Ramnad District irrespective of the fact whether they are members of the Association or not. It is our fond hope that at least in the future there will be better response from the medical men in and around the district to our notice of meetings.

The Association has, as a rule, provided light refreshments at the commencement of its sittings when no one offered to be the host at meetings held at Karaikudi. The Association is deeply indebted to the authorities of the S. M. S. High School, Karaikudi for having placed the first floor of the school at its disposal for holding meetings.

The interdistrict fellowship between our Association and those of neighbouring districts originally initiated by the Hon'ble Dr. T. S. S. Rajan who was instrumental in the founding of our Association, have been marked this year, in as much as the associations of Madura, Tinnevelly, Trichinopoly and Pudukotah have taken part in our meetings. There were three special meetings, out of which two were joint meetings of Ramnad and Madura Associations once held at Madura and the second time at Ramnad; on both these occasions those assembled were entertained to tea and dinner. The third was

a very successful combined meeting of Tinnevelly, Ramnad and Madura Associations held at Sourashtra High School, Madura, under the auspices of the Madura Medical Association. There was a Veena performance and tea before the meeting which was attended by over 133 doctors. After dinner the members of the Madura Medical Association staged a drama in Tamil in which some of our members also participated.

This year was a land mark in the history of this Association. This Association, which was affiliated to the Indian Medical Association, has been converted into a Branch of the Indian Medical Association. By this move every regular member of this Association by paying Rs. 7 per year becomes automatically a member of the Indian Medical Association with eligibility for voting in both the Associations and to get a copy of the Journal of the Indian Medical Association direct from Calcutta. In order to enable a greater number of medical men to take part in our meetings, a second class of membership—the associate member, has been formed this year who pay a subscription of Rs. 4 per year and have no vote in business matters.

The vigorous activity of the Association during the year was due to the harmony and active co-operation from the neighbouring Associations of Madura and Tinnevelly.

The year opened with a cash balance of Rs. 679-0-2 and the closing balance is Rs. 514-12-2.

Among the several resolutions passed during the year the following deserve notice:—

The combined meeting of the Tinnevelly District, Ramnad District and the Madura Medical Associations request the Ministry of Public Health to the Government of Madras to encourage the Indian medical industries by insisting the Medical Stores Depot to purchase their requirements from Indian made goods.

This meeting of the Ramnad District Medical Association requests the Government that in the new Madras Medical Council Act to be passed by the Madras Legislature, in the elected members to the Council proper and proportionate representation of the following groups of practitioners—1 Independent medical practitioners, 2 Rural medical practitioners and 3 Municipal and Local Board employees—be given in the election according to their electoral strength.

This Association requests the Government that they may be pleased to provincialise the services of the medical officers under Local Boards and Municipalities as in the case of other officers connected with local bodies.

I avail of this opportunity to tender my hearty thanks to the President of the Association Captain B. Dayananda Rao, District Medical Officer, Ramnad and other members of the managing committee but for whose unfailing courtesy and support it would not have been possible for me to discharge my duties to your satisfaction.

It is our fervent prayer that this Association with the hearty co-operation of the service and non-service men of the district will be of great benefit to the medical profession and thereby to the community at large.

K. S. SRINIVAS, L.M. & S.
Secretary.

STATEMENT OF MEETINGS HELD DURING THE YEAR ENDING, 31ST. MARCH, 1938.

Date.	Lecturer.	Subject.
10-4-1937—	(i) R. Kalamegam.	(i) Traumatic Affections of joints.
	(ii) Rao Bahadur S. Padmanabha Sarma.	(ii) Empyema.
	(iii) Rao Bahadur T. S. Tirumurthi.	(iii) Modern conception of pathology of Bright's Disease.
22-5-1937—	Captain B. Dayananda Rao.	Anæmias of Pregnancy.
19-6-1937—	M. N. Rajan.	Our interest in Cardiology.
24-7-1937—	J. R. Moses.	Transverse Presentation in the moffussil.
28-8-1937—	T. S. Shetty.	Tympanic membrane and its pathology.
18-9-1937—	M. Nagaswami.	Meningitis—Tubercular.
23-10-1937—	(i) H. S. Thomas.	(i) Nutrition.
	(ii) R. Krishnaswami.	(ii) Incidence of Malaria in Cumbum Valley.
20-11-1937—		Discussion on recommendations of the Executive Committee.
18-12-1937—		Passing of the recomendations of the Executive Committee.
4-1-1938—		Discussion on the scheme of Honorary medical officers (special committee appointed to report on this subject).
19-2-1938—	Sister K. Wilcke, R. N.	Some Thoughts regarding the nursing profession in India.
19-3-1938—		Discussion on Rural Medical Aid and send off to Dr. Shetty.

At a meeting dated 4-1-38 Professor Rudolf Demel of Vienna University should have lectured on "Treatment of Acute Suppurative and Phlegmonous diseases." But he could not attend the meeting as he was detained at Dhanushkodi Pier under unforeseen and unavoidable circumstances and could not reach Kanadukathan.

There were eleven monthly meetings, four meetings of the Executive Committee, two meetings of the General Body and one special Committee Meeting during the year.

The average attendance at the meetings is 28·9. Case reports were discussed and some cases demonstrated at these meetings.

TINNEVELLY BRANCH

The Tinnevelly District Medical Association held its monthly meeting on Saturday, the 25th of June, 1938, at Papanasam, one of the most sacred places of the district, noted for wild scenery and most charming waterfalls.

Members numbering 42 gathered from all parts of the district. All the members had an early bath in the falls which was followed by light refreshments.

The meeting began at 10 a.m. under the Presidentship of Lieut. Col. T. S. Shastry, I.M.S. The Secretary, read the minutes of the last monthly meeting held at Mangalagiri,.

The proposal of the Ramnad Branch of the Indian Medical Association that a Presidency Branch of the I. M. A. should be formed in order to be able to speak in the name of the whole of the Presidency in regard to the I. M. A., was discussed and the following resolution was unanimously passed:—

The Tinnevelly District Medical Association is of opinion that the question of forming a Provincial Branch of the I. M. A. for the Madras Presidency may be considered when an adequate number of District Branches of the I. M. A. have been formed in the Presidency.

The letter from the Secretary, Indian Medical Association, Calcutta, regarding the All-India Anti-Medical Council Act Day was read out and discussed. The following resolutions were passed *nem con.*:—

"The Tinnevelly District Medical Association is of opinion that the time has come when the All-India Mdical Licentiates Association and its Branches together with its membership, funds, and Journal should be entirely amalgamated and merged with the Indian Medical Association, thereby facilitating the formation of a united front for the redress of the legitimate grievances of the Licentiates and to unify the Allopathic Medical Profession as a whole."

The following resolution was also passed unanimously:—

The Tinnevelly District Medical Association is of opinion that the Indian Medical Association subscription may be reduced from Rs. 3/- to Rs. 2/- inasmuch as the membership of the Indian Medical Association has increased appreciably since its formation and as there is every likelihood of more Medical Associations joining the Indian Medical Association if the subscription is reduced and that this suggestion may be sent up to the Central Council of the Indian Medical Association.

It was also considered necessary to discuss the above subjects at Courtallam meeting on the 23rd of July, 1938, where the Medical Association of the Travancore State, Ramnad, Madura and Tinnevelly meet together.

Dr. T. K. Nilakanta Iyer, Selection Grade Sub-Assistant Surgeon of the Government Headquarters Hospital, Palamcottah, read out notes on the following interesting cases which were successfully operated and treated at the Government Headquarters Hospital, Palamcottah:—

1. A case of stab injury of the neck.
2. A case of liver abscess.
3. Two cases of septic knee—successful treatment with Proseptasine and Soluseptasine.
4. Three cases of erysipelas—successful treatment with Prontosil.
5. A case of facture of femur attended with hæmatomyelia.

After detailed discussion by the members Colonel Shastry, summed up the salient and important features of all cases. He offered his cordial thanks to all those members who helped towards the success of the function and thanked Dr. T. V. Gopal Menon, M.B.B.S., for the excellent arrangements. He congratulated Dr. K. R. Venkoba Rao, L.M. & S. H.Sc., one of the members of the Association, for his selection for the Health Department of Madras.

All had an excellent dinner at 1 p.m. Thereafter an enjoyable musical entertainment brought the happy gathering to a close at 3 p. m.

HEALTH EXHIBITION

At 5 p. m. a very enthusiastic Health Exhibition was held at the Thirthapathi High School, Ambasamudram. Dr. T. C. Sankara Iyer, L.M.P. of Kallidaikurchi, presided over the function.

Lieut. Col., T. S. Shastry, I.M.S., the President welcomed the guests and requested Mr. Jayarajan, I.C.S., Sub-Collector, Sermadeir, to open the Health Exhibition. Mr. Jayarajan in declaring the Exhibition open said that such exhibitions are very useful and beneficial to the masses.

The President delivered his speech in Tamil which was very interesting. He impressed the necessity of such exhibition and its usefulness, and urged the people to practise the ways of health and to create a health conscience and stressed how our personal habits should be improved in regard to our latrines and watercourses.

The Exhibition was open to the public and school children till late in the evening. The exhibits consisted of posters relating to cholera, tuberculosis, malaria, small-pox, etc. This was very much appreciated by the gathering which consisted mostly of school boys and teachers—about 300 strong—from the whole Ambasamudram area.

Lieut-Col., T. S. Shastry, I.M.S., offered cordial thanks to the Head-Master, Thirthapathi High School, Mr. Jayaranjan, I.C.S., and Dr. T. C. Sankara Iyer for their kind co-operation for the success of the Health Exhibition.

K. RAMA AYYAR, M.B.B.S. (Andhra),
Secretary and Treasurer.

FARIDPUR MEDICAL ASSOCIATION

The following resolutions amongst others were passed at a meeting of the Association held on the 21st June, 1938.

Resolved unanimously that no members of the Association shall examine any case for life assurance companies whose scales of fees are below rupees eight only for one thousand rupees or for any amount less than that.

Considered the letter dated 12-6-38 of the Joint Secretary, Indian Medical Association (Bengal Provincial Branch) and resolved that our Association is desirous of holding the 2nd session of Bengal Provincial Medical Conference at Faridpur in November next.

SATYARANJAN GHOSE,
Hony. Secretary.

HOOGHLY, CHINSURA AND CHANDERNAGORE BRANCH

The second General Meeting of the branch took place on 29-5-38 at its office "Sunny Bank" with all its members present.

The Secretary read his report for the year 1937-38 which is as follows:—

By the grace of God our Association has completed the initial year of its existence. It is only meet and proper that we should look back to take stock of our efforts put in by way of realisation of the views and ideals we had set forth before us.

THE INAUGURAL MEETING

The Association was brought into being under the happiest auspices. Dr. N. R. Sen Gupta, M.D., one of the most distinguished members of the profession in the province came down all the way from Calcutta to preside over the inaugural meeting on the 30th April, 1937. He was accompanied by Dr. T. N. Ghosh, the Organising Secretary of the Provincial Headquarters. It was attended by no less than 30 members of the profession hailing from different parts of Hooghly, Chinsura, Chandernagore and other parts of the district. The enthusiasm and keenness evinced at the meeting were very encouraging. The executive body of seven members with powers to co-opt in addition to the following office-bearers was elected:—

President—Dr. M. N. Chakrabarty.

Vice-Presidents—Dr. J. Sreemany and Capt. J. C. Dey.

Secretary—Dr. S. C. Ghose.

Jt. Secretary—Dr. S. K. Sen Gputa.

Asst. Secretary—Dr. K. Seal.

Treasurer—Dr. M. M. Chatterjee.

Executive Committee:—Dr. Miss Lalita Roy, Capt. K. N. Chatterjee, Drs. Balai Chand Seal, N.

N. Konar, Bankim Chatterjee, Shyama Pada Roy and Nagendra Nath Dey were co-opted.

The President, Dr. Sen Gupta, delivered an inspiring and illuminating address on the vital problems affecting the profession.

Enrolment:—We have on the roll of this branch 26 members, a feat well to be proud of when we take in stock the short period of the existence of the branch and the acute economic distress through which the country in general and our profession in particular is passing. This, in no small measure, is due to the efforts of the sub-committee formed to enrol members. Though the strength of our enrolment compares favourably with other branches, there is still room for improvement. We must not forget that we of this profession are a disjoined and disorganised body. The Government through the creation of compartment in the services has divided us against ourselves and that hydra-headed monster the caste-system that has eaten into the vitals of the Hindu society has unobtrusively spread its tentacles round our profession. Finding us weak and disunited a constant war is being waged against us on all fronts by the quacks and devotees to other systems of medicine and we are losing ground everywhere. The only effective course to stem this rot is to gather under the banner of an All-India Body, the Indian Medical Association and unfurl the banner of camaradery.

Meetings:—We had as many as 7 General meetings including the inaugural one, 2 Executive Committee meetings and 4 clinical meetings. In the general meetings this Association voiced its strong disapproval of the practice of recruitment in I. M. S. through nomination and strong protest against the reservation of the special posts in colleges and research work for British officers and its demand of the complete abolition of the civil side of the I. M. S.

The Association recorded its strong protest against nonrecognition by the G. M. C. of the M. B.'s of the Calcutta University from 1924-36.

The Association also voiced its strong protest against the exclusion of the licentiates who form the bulk of the profession in India from the Register of the Indian Medical Council.

The Association drew up a scheme for the relief of the unemployment in the medical profession. Dr. K. Seal, gave an outline of the scheme and Dr. B. Chatterjee, our representative to the Central Council, read a paper on the subject and drew up a skeleton scheme on which a discussion followed.

At the special invitation of Major Fitch, the then Civil Surgeon, the following four members of the Association volunteered their services to conduct ambulance classes:—

(1) Capt. K. N. Chatterjee.
(2) Dr. Dasarathi Ghosh.
(3) Dr. Kartick Chandra Mallick and
(4) Dr. Bibhuti Bhusan Chakrabarty.

A sub-committe composed of 8 members was appointed to consider the scheme of leprosy and maternity clinics formulated by the H. C. Municipality. The sub-committee pointed out the defects of the scheme and submitted an alternative scheme.

Another sub-committe of 6 members was also appointed to deal with the provision of the Health Insurance Bill of Mr. Shib Nath Banerjee, M.L.A. The sub-committee's report embodied the various alternatives suggested by the Association.

Clinical Meetings:—We had four clinical meetings and we have to thank Capt. J. C. De who initiated the debate on the group of typhoid fevers and their treatment. His clear and thorough grasp on and the approach to the subject from all angles and his lucid exposition were a rare treat and we hope we shall not be deprived of such treats in future.

Central Council:—Our Association was represented in the Central Council by Dr. B. Chatterjee and Dr. M. M. Chatterjee; the former, as noted before in this report, attended the Delhi sitting and took part in the discussion on unemployment scheme there.

Provincial Council:—The following gentlemen represented this Association in the Provincial Council:—(1) Capt. J. C. De, (2) Dr. M. Chatterjee and Dr. B. K. Ghose. When Dr. M. Chatterjee moved to the Central Council, Dr. S. K. Sen Gupta stepped in.

Our Association nominated the following members for studies in T. B. work:—

(1) Dr. S. K. Guha, (2) Dr. B. Chakraborty, (3) Capt. K. N. Chatterji, (4) Dr. S. P. Chatterji and (5) Dr. K. Seal.

Gentlemen, these are the feats performed by the Association in its early infancy and a feat not to be

ashamed of. But more remains to be done. We have not yet succeeded in getting into our fold the vast bulk of the cream of the profession and we should not rest on our oars till that is accomplished.

Finance:—The Treasurer Dr. M. Chatterjee is placing the audited account before you for your confirmation and consideration. You will find from that we are not a very prosperous body and unless we can enrol more members we shall have to live in precarious existence. Gentlemen, remember, nowadays blessed are they who possess a fat purse and a big bank balance.

Now the last and the concluding item that I am coming to is a very pleasant one. The Association records its grateful thanks to Capt. R. Sinha for his sporting offer of accommodating the office of this Association in the elegantly furnished study of his residence. Gentlemen, we have been enjoying his hospitality every month and the dainty dishes that we have been regarded to, have an added incentive to our meeting so frequent at his place. This Association is also grateful to one of our Vice-presidents Dr. Sreemany for his generous gift of a table, two chairs and an almirah. We still remember with longing and lingering to take his hospitality at his residence where the first executive meeting was held.

This Association is grateful to our Secretary, Dr.S. C. Ghosh for his kind offer of a monthly sum of Rs.3/- towards the pay of a part-time office assistant.

This Association is deeply indebted to Dr. K. Seal, the Asst. Secretary who is indefatigable in his efforts to further the cause of this Association and who practically ran the Secretariate of this Association.

* * *

The following are the office-bearers for the year 1938-39:—

President—Capt. J. C. Dey, I.M.S. (Retd.).

Vice-Presidents—Drs. J. Sreemany and N. K. De.

Secretary—Dr. S. C. Ghose.

Jt.Secretary and Treasurer—Dr. M. M. Chatterji

Asst. Secretaries—Drs. S. C. Guha and S. Bhandari

Executive Committee:—Drs. Miss L. Roy, S. Chatterji, S. P. Roy, N. N. Konar, B. Chakraborty and S. C. Roy.

With a vote of thanks to the chair, the meeting terminated.

* * * *

Resolutions passed at the General Meeting held on 26-6-38:—

1. That the holding of the Provincial Conference be provisionally accepted and final confirmation be settled at the next meeting.

2. A sub-committee consisting of the following members be formed to enlist more members:—

Dr. S. C. Guha, Dr. K. Mallick, Dr. S. P. Roy, Dr. M. Chatterjee and Dr. N. K. De.

3. A letter of thanks be sent to Dr. J. Sreemani for his kind donations of Rs. 25/- already paid for the furniture of this Association.

4. That Part V of the Gazette of India dated 9th April, 1938, be obtained from the Manager of Publications, Delhi, before a considered opinion be given respecting the Indian Income-Tax Amendment Bill, 1938.

5. That a General Meeting be called requesting all members of the profession to attend to vehemently protest against the provisions of the Indian Medical Act in disregarding the licentiates from being registered under the said Act.

MOHINI M. CHARTTERJEE
Jt. Secretary.

MEDICAL NOTES AND NEWS

PROPOSAL TO PUNISH FEE SPLITTING AND ADVERTISING

A public hearing will take place shortly before one of the committees of the French senate on a bill introduced by a former minister of public health, Mr. Sellier. The object of the proposed law is to penalize not only physicians who divide the fees received from patients referred to them for an opinion or operation but to put a stop to rebates given by orthopedic apparatus makers and druggists to physicians who send their patients. The Federation of Medical Syndicates, which has more than 20,000 members and look after public relations for the entire medical profession here, passed resolutions in 1932 condemning fee splitting in any form. At the meeting of the federation on February 20th, the statement was made that many physicians have refused to divide the fees received from the patients with the practitioner who sent them but that the application of this principle was not as widespread as might be wished for.

Another objective of the proposed Sellier law is an attempt to prevent newspapers from accepting advertisements of treatments by quacks. The extent to which such claims by quacks of all description appear in journals here is beyond all imagination. The ethical standard of the lay press in this country, as regards this matter, is much below that of reputable newspapers in other countries. Advertising by quacks is such a lucrative source of income that the proposed Sellier law to penalize it will meet with a great deal of opposition. (*Journal of American Medical Association*).

RESEARCH ON CONDITIONS DUE TO LOW TEMPERATURES

A centre of research on the pathology and therapy of conditions due to the low temperatures of mountain regions has been established at Genoa. The activities concern research on thermal adaptation of man and animals of low temperatures, the pathology and treatment of lesions due to cold, particularly the use of short wave therapy, and the prophylaxis of such lesions, especially as the latter occur in the army and in connection with winter sports. Professor Sabatini, director of the new centre, has obtained the collaboration of the army sanitary corps. Besides assigning a major of the medical corps to participate, the general staff of the army sanitary corps has ordered that soldiers severely enough effected with lesions due to cold to require hospitalization should be sent to the Military Hospital at Genoa, where special accommodations will be reserved. (*Journal of the American Medical Association*).

COMMISSION OF PHARMACOPOEIAL EXPERTS

The Technical Commission of Pharmacopoeial Experts, appointed by the Council of the League of Nations at its meeting in January last, met at Geneva in May. The Commission's task was to prepare a programme of studies, choose suitable drugs for examination, and determine a uniform method of analysis, assay, and preparation of the drugs selected. The necessity for such work arises from the difficulties encountered by pharmacists in dispensing prescriptions for travellers from foreign countries and in the replenishment of medicine chests of ships at ports of call. Unification would, in addition, be of great advantage to manufacturers and would assist in the comparability of the results of medical treatment in different countries. The Commission prepared a list of the more important drugs which it proposed to study and codify. Draft schemes for the preparation of monographs on the drugs were agreed upon, and a number of general priniciples were settled. The list of drugs was divided amongst the members of the Commission for the purpose of study in collaboration with experts in their own countries. (*British Medical Journal*).

DEDICATION OF MONUMENT IN MEMORY OF PROFESSOR CALMETTE

The city in which the late Professor Calmette was born has honored his memory by the erection of a monument, which was unveiled at Nice, April 8.

The work depicts a nurse administering the BCG vaccine to an infant, which she holds in her arms. On the side of the monument is a plaque of the distinguished bacteriologist, who during the last years of his activity at the Pasteur Institute of Paris devoted his energies to the prevention of tuberculosis in the newborn by means of BCG vaccine. (*Journal of the American Medical Association*).

A NEW MATERNITY HOME

The Calcutta Corporation recently gave administrative sanction to the plan and estimate amounting to Rs. 44,000 for the construction of a new and up-to-date maternity home at 35, Ekbalpore Road. (*Calcutta Municipal Gazette*).

THE PRESIDENCY OF THE ROYAL COLLEGE OF PHYSICIANS

The office of president of the Royal College of Physicians has been held by Lord Dawson for the unusually long period of seven years, during which time he directed the activities of what was formerly considered simply an academic body into such practical directions as the promotion of research and post-graduate education. He has been succeeded by Dr. Robert Hutchison, consulting physician to the London Hospital and the Hospital for Sick Children, who is a well known clinical teacher and an authority on dietetics and pediatrics. His successful text-books include the "Index of Treatment" (of which he is editor), "Clinical Methods," "Food and Dietetics" (which has reached an eighth edition), "Lectures on Diseases of Children" (which has reached a seventh edition), and "Elements of Medical Treatment" (third edition). In an age of faddists, in which the craze for novelty leads to the acceptance of much which is unsound, the new president is distinguished for his sturdy commonsense. He is a Scot from the University of Edinburgh. (*Journal of the American Medical Association*).

LISTER MEDAL

The Lister Medal for 1939, which is awarded in recognition of distinguished contributions to surgical science, has been granted to Professor Rene Leriche, professor of clinical surgery in the University of Strasbourgh, and he will deliver the Lister Memorial Lecture in 1939 at the Royal College of Surgeons of England. This is the sixth occasion of the award, which is made by a committee representative of the Royal Society, the Royal College of Surgeons of England, the Royal College of Surgeons in Ireland, the University of Edingburgh, and the University of Glasgow. Previous Lister mediallists have been Sir William Watson Cheyne, Professor Anton Von Eiselsberg, Professor Harvey Cushing, Sir Charles Ballance, and Sir Robert Muir.(*British Medical Journal*).

SWINEY PRIZE FOR A WORK ON MEDICAL JURISPRUDENCE

The next award of the Swiney Prize will be made in January, 1939, on the ninety-fifth anniversary of the testator's death. Dr. Swiney died in 1844, and in his will he left a sum of money to the Royal Society of Arts for the purpose of presenting a prize on every fifth anniversary of his death, to the author of the best published work on Jurisprudence. The Prize is a cup, of a value of £100, and money to the same amount.

The award is made by a Joint Committee of the Royal Society of Arts and the Royal College of Physicians, which appoints special adjudicators.

The Prize is offered alternately for Medical and General Jurisprudence, but if at any time the Committee is unable to find a work of sufficient merit in the class whose turn it is to receive the award, it is at liberty to recommend a book belonging to the other class. On the last occasion of the award (1934) the Prize was awarded for General Jurisprudence. It will, therefore, be offered on the present occasion for Medical Jurisprudence.

Any person desiring to submit a work in competition, or to recommend any work for the consideration of the Judges, should do so by letter, addressed to the Secretary of the Society, not later than November 30th, 1938.

List of Former Recipients

1849 J. A. Paris, M.D. and J. Fonblanque, for their work, "Medical Jurisprudence."

1854 Leone Levi, for his work, "The Commercial Law of the World."

1859 DR. ALFRED SWAYNE TAYLOR, F.R.S., for his work, "Medical Jurisprudence."

1864 HENRY SUMNER MAINE (afterwards K.C.B.), D.C.L., for his work, "Ancient Law."

1869 WILLIAM AUGUSTUS GUY, M.D., for his "Principles of Forensic Medicine."

1874 THE RIGHT HON. SIR ROBERT JOSEPH PHILLIMORE, D.C.L., for his "Commentaries on International Law."

1879 DR. NORMAN CHEVERS, for his "Manual of Medical Jurisprudence of India."

1884 SHELDON AMOS, M.A., for his work, "A Systematic View of the Science of Jurisprudence."

1889 DR. CHARLES MEYMOTT TIDY, F.C.S., for his work, "Legal Medicine."

1894 THOMAS ERSKINE HOLLAND (afterwards Sir), K.C., D.C.L., for his work, "The Elements of Jurisprudence."

1899 DR. J. DIXON MANN, F.R.C.P., for his work, "Forensic Medicine and Toxicology."

1904 SIR FREDERICK POLLOCK, BT., and PROFESSOR F. MAITLAND, for their work, "The History of English Law before Edward I."

1909 DR. CHARLES MERCIER, F.R.C.P., F.R.C.S., for his work, "Criminal Responsibility."

1914 JOHN W. SALMOND, K.C., for his work, "Jurisprudence."

1919 DR. CHARLES MERCIER, F.R.C.P., F.R.C.S., for his work, "Crime and Criminals."

1924 PROFESSOR SIR PAUL VINOGRADOFF, F.B.A., for his work, "Outlines of Historical Jurisprudence."

1929 PROFESSOR SYDNEY SMITH, M.D., for his work, "Forensic Medicine."

1934 PROFESSOR SIR WILLIAM S. HOLDSWORTH, K.C., for his work, "A History of English Law."

CORRESPONDENCE

The Editor is not responsible for any views expressed by the contributor.—ED.

The Editor,

Journal of the I. M. A.

Dear Sir,

I have read with interest the reply of Dr. Seal to my letter on the subject of the new Rules regarding the passing of the budget by the Central Council, in the correspondence column of your Journal (*vide* May, 1938 issue, page 490).

No two institutions in this world, be they political, social, commercial or otherwise, are in their constitution exactly similar or parallel to each other, as no two blades of grass are equal. One has to study carefully the constitution of a particular body or association in order to understand and grasp the meaning and principles underlying its rules and regulations.

The constitution and government of the Indian Medical Association are the same in essence and spirit both under the new and the old rules, and an attentive consideration of them will show that the new rules have introduced no new innovations or departures from the old practice, but have simply clarified and amplified them in greater detail.

Under the old (altered) Rule 7 (b), it will be seen that the Branch Associations were autonomous bodies, who were free to enrol members paying subscriptions according to denominations fixed by the Branches. They had only to remit to the Central Council Rs. 3/- per head of their members. Under the old Rule 20 the general management of the I M. A. was solely vested in the Central Council and under Rule 31, the Central Council was empowered to defray all expenditures of the I. M. A.

The position under the old rules was, therefore, the same as under the new rules [*vide* Rules 6 D(c), 10 A(c), 15 & 16 (B)]. The local Branches were quite independent in the management of their finances and the I. M. A. had no voice in their budgets. Nor was the I. M. A. liable for any of their debts or liabilities of its Branches. But because the Branches paid a certain portion of their income from subscriptions received from their members, they were given the right to elect their representatives to the Central Council according to certain ratio to their number of membership, *vide* old Rule 20(2) and new Rule 15 B(a). The individual members of the Branches, it should be remembered, *have no direct concern with the I. M. A.* and do not pay directly any subscription as direct members who have to pay subscription of Rs. 12/- per year. Of course Dr. Seal is right when he says that the position of direct members is anomalous because they are given no right of representation in the Central Council. In my opinion the rules do need amendment in this respect and ample representation should be given to them on the Central Council. But Dr. Seal forgets the fact that the Branch members are members of the Branch, and the Branch, like a corporate body, makes a contribution on their behalf to the I. M. A. and secures for them *the privilege of obtaining advantages of its objects of the I. M. A.* as laid down in Rule 2. Because the Branches make contributions, they have been given *the right to elect representatives on the Central Council.* But there is no reason or justification for the proposition that individual members of these Branches should have a right in the management of the finances of the I. M. A., when they are not liable for any of the debts and liabilities of the I. M. A. [*vide* Rule 6 D(d)], nor when do they pay subscription directly to the I. M.A. It is just like the illegal and absurd demand of a person who without paying subscription to a club or association wants to have a share in its management.

The utterance of Dr. B. C. Roy quoted by Dr. Seal that "with regard to all the questions of liabilities of the Association, it is not the Central Council that is responsible, the whole Association is responsible" is apparently based upon a misapprehension. According to the constitution of the I. M. A., if by "the whole Association" is meant the individual members of the Branches, then the facts are just the reverse. The individual members of the Branches are *not* responsible for any debts or liabilities of the

I. M. A. It is the Central Council of the I. M.A. that is responsible.

In one place Dr. Seal has come near the truth when he says that "the local branches are the part and parcel of the I. M. A." Although not "part and parcel of the I. M. A." they are the constituents of the I. M. A. and therefore the local Branches who (as corporate bodies) are "tax-payers" to the I. M. A. have been given the right of representation to the Central Council. But one labours under a confusion of ideas when he includes in the term "local Branches" the individual members thereof—who are not "tax-payers" to the I. M. A. Discussion with my friends which followed Dr. Seal's letter in your Journal has enlightened me on the point as above.

I trust I have sufficiently elucidated the point under controversy, and would ask every one interested in point to study the rules and constitution of the I. M. A. carefully and I am sure that they will agree with what has been written above.

I might again say that in view of what I have already said that Annual General Meeting is likely to be dominated by the members of the Branch or Branches of the Province where the Annual General Meeting takes place, it is far more expedient and would safeguard the interests of other Provinces, if the function and power of formation of Annual Budget remains vested in the Central Council.

MEERUT,
July 10, 1938.

Yours truly,
R. N. BOSE, M.B., CAPT.

* * *

THE EDITOR,
Journal of the I. M. A.

DEAR SIR,

I shall be obliged if you will publish the following communication in your esteemed Journal.

MEERUT,
July 16, 1938.

Yours truly,
R. N. BOSE, M.B., CAPT.

XV ALL-INDIA MEDICAL CONFERENCE, MEERUT

Dear Doctor,

The next All-India Medical Conference is holding its 15th session in Meerut during the Christmas week.

Besides the General Section and the Exhibition, there will be a Scientific Section where original papers will be read and discussed thus affording an excellent opportunity for members to exchange opinions with members of the profession working in different parts of India. May I, therefore, request you to contribute a paper and take part in the discussions?

The scale of fees are as follows:—

(1) Membership of Reception Committee Rs. 10/-

(2) Delegate from a Branch of the Indian Medical Association Rs. 5/-

(3) Other member of the Indian Medical Association attending the Conference Rs. 5/-

(4) Non-member of the Indian Medical Association attending the Conference Rs. 8/-

Any medical man or other scientist can also take part only in Scientific Section on payment of a fee of Rs. 5/- only.

If you intend to contribute a paper, a typed copy of the same with an abstract of not more than 200 words and your membership fee may be sent to me. I shall, however, be glad if you will let me know the title of your paper as soon as possible. There will also be Sub-sections of the different branches of medical science. If you want any special arrangements to be made in connection with your paper, please let me know in good time.

The papers will be the property of the Indian Medical Association and will be published in the Journal of the Indian Medical Association at the discretion of the Editor.

May I also request you to enlist the co-operation of your colleagues whom we have not been able to reach.

Thanking you.

Yours fraternally,

CAPT. R. N. BOSE, M.B.
Organising Secretary,
XV All-India Medical Conference.